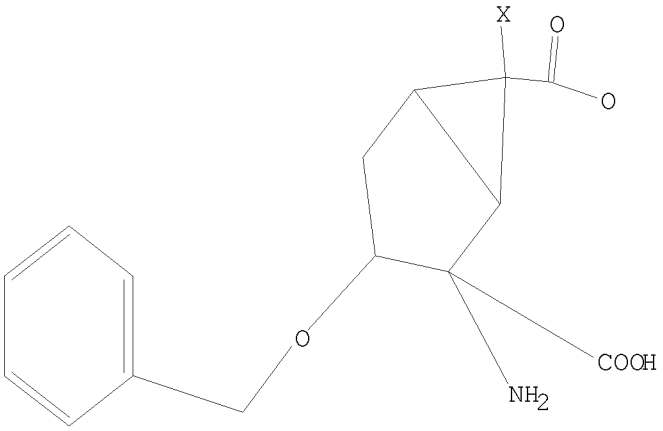
10/562,018

eries\10562018.str

L1 STRUCTURE UPLOADED

=> d
L1 HAS NO ANSWERS
L1 STR



Structure attributes must be viewed using STN Express query preparation.

=> s l1 ss sam
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Substance data SEARCH and crossover from CAS REGISTRY in progress...
Use DISPLAY HITSTR (or FHITSTR) to directly view retrieved structures.

SAMPLE SEARCH INITIATED 16:14:47 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED - 15 TO ITERATE

100.0% PROCESSED 15 ITERATIONS 6 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 68 TO 532
PROJECTED ANSWERS: 6 TO 266

L2 6 SEA SSS SAM L1

L3 5 L2

MISSING OPERATOR L3 SS

TOh 09/09/2009

The search profile that was entered contains terms or
nested terms that are not separated by a logical operator.

=> s l1 sss sam
   REG1stRY INITIATED
Substance data SEARCH and crossover from CAS REGISTRY in progress...
Use DISPLAY HITSTR (or FHITSTR) to directly view retrieved structures.

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SAMPLE SCREEN SEARCH COMPLETED - 15 TO ITERATE

100.0% PROCESSED 15 ITERATIONS 6 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 68 TO 532
PROJECTED ANSWERS: 6 TO 266

L4 6 SEA SSS SAM L1

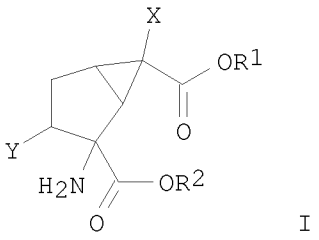
L5 5 L4

=> d 1-5 ibib abs hitstr
THE ESTIMATED COST FOR THIS REQUEST IS 28.20 U.S. DOLLARS
DO YOU WANT TO CONTINUE WITH THIS REQUEST? (Y)/N:y

L5 ANSWER 1 OF 5 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2006:733075 CAPLUS
DOCUMENT NUMBER: 145:188474
TITLE: Preparation of 2-amino-bicyclo[3.1.0]hexane-2,6-dicarboxylic acid ester derivatives as group II metabotropic glutamate receptor antagonists
INVENTOR(S): Yasuhara, Akitaka; Sakagami, Kazunari; Ota, Hiroyuki; Nakazato, Atsuro
PATENT ASSIGNEE(S): Taisho Pharmaceutical Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 95 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
JP 2006193507	A	20060727	JP 2005-330903		20051115
PRIORITY APPLN. INFO.:			JP 2004-363690	A	20041215

OTHER SOURCE(S): MARPAT 145:188474
GI



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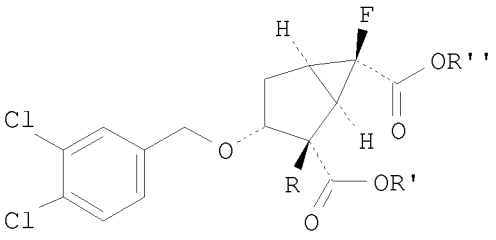


II

AB Title compds. I [R1, R2 = alkyl, alkenyl, alkynyl, etc.; X = H, F; Y = -OCHR3R4, -SR3, -S(O)nR5, etc.; R3, R4 = H, alkyl, alkenyl, etc.; R5 = alkyl, alkenyl, Ph, etc.; n = 1, 2], pharmaceutically acceptable salts or hydrates thereof were prepared For example, reduction of compound II [R = N3; R', R'' = Et], e.g., prepared from (1R,5R,6R)-6-fluoro-2-oxobicyclo[3.1.0]hexane-6-carboxylic acid Et ester in 6 steps, followed by hydrolysis using LiOH and SOCl2 mediated esterification with methanol afforded compound II [R = NH2; R' = H; R'' = methyl] hydrochloride. Compound II [R = NH2; R' = H; R'' = methyl] hydrochloride showed antidepressant effects in rat forced swimming test. Compds. I are claimed useful for the treatment of depression.

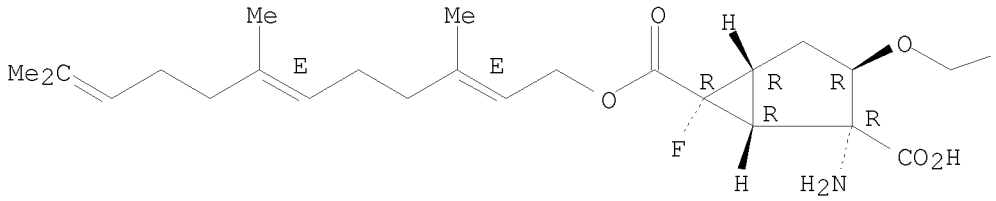
IT 820244-11-9P 820244-46-0P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 2-amino-bicyclo[3.1.0]hexane-2,6-dicarboxylic acid ester derivs. as group II metabotropic glutamate receptor antagonists for treatment of depression)

RN 820244-11-9 CAPLUS

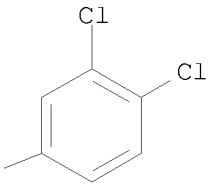
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-3-[(3,4-dichlorophenyl)methoxy]-6-fluoro-, 6-[(2E,6E)-3,7,11-trimethyl-2,6,10-dodecatrien-1-yl] ester, (1R,2R,3R,5R,6R)- (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A

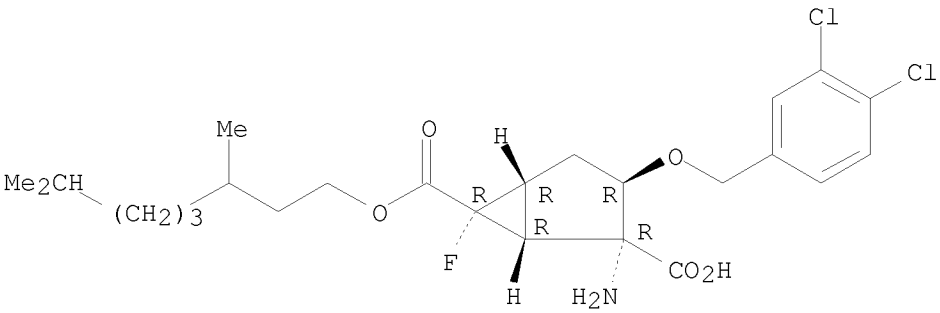


PAGE 1-B



RN 820244-46-0 CAPLUS
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-3-[(3,4-dichlorophenyl)methoxy]-6-fluoro-, 6-(3,7-dimethyloctyl) ester, (1R,2R,3R,5R,6R)- (CA INDEX NAME)

Absolute stereochemistry.



L5 ANSWER 2 OF 5 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2005:14355 CAPLUS
DOCUMENT NUMBER: 142:113634
TITLE: Preparation of 2-aminobicyclo[3.1.0]hexane-2,6-dicarboxylic acid esters as Group II metabotropic glutamate receptor antagonists
INVENTOR(S): Yasuhara, Akito; Sakagami, Kazunari; Ohta, Hiroshi; Nakazato, Atsuro
PATENT ASSIGNEE(S): Taisho Pharmaceutical Co., Ltd., Japan

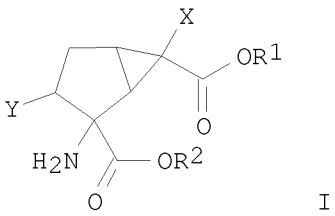
SOURCE: PCT Int. Appl., 144 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005000791	A1	20050106	WO 2004-JP9398	20040625
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2004252017	A1	20050106	AU 2004-252017	20040625
CA 2530706	A1	20050106	CA 2004-2530706	20040625
EP 1637517	A1	20060322	EP 2004-746867	20040625
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR				
CN 1812960	A	20060802	CN 2004-80017917	20040625
BR 2004011823	A	20060808	BR 2004-11823	20040625
US 20070021394	A1	20070125	US 2004-562018	20040625
RU 2349580	C2	20090320	RU 2006-101273	20040625
ZA 2005010124	A	20061129	ZA 2005-10124	20051213
MX 2005013740	A	20060517	MX 2005-13740	20051215
IN 2005CN03529	A	20070525	IN 2005-CN3529	20051226
NO 2006000428	A	20060310	NO 2006-428	20060126

PRIORITY APPLN. INFO.:
JP 2003-181930 A 20030626
JP 2003-373511 A 20031031
JP 2004-128663 A 20040423
WO 2004-JP9398 W 20040625

OTHER SOURCE(S): MARPAT 142:113634

GI



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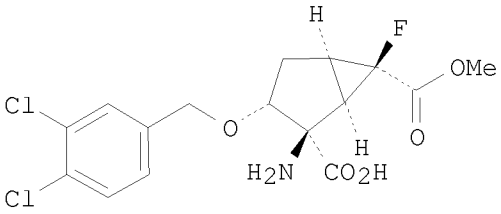


II

AB The title compds. I [wherein R1 and R2 = independently alkyl, alkenyl, alkynyl, etc.; X = H or F; Y = (un)substituted alkoxy, SH, amino, etc.] or hydrates or pharmaceutically acceptable salts thereof are prepared as Group

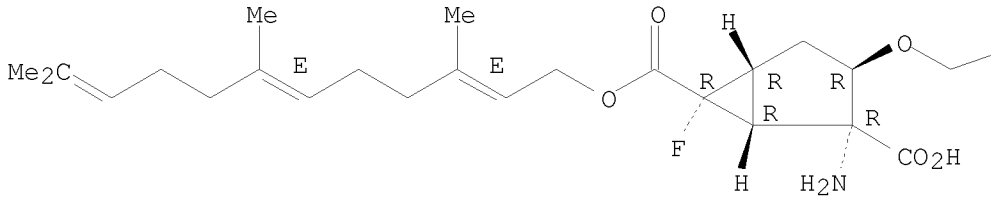
II metabotropic glutamate receptor antagonists. For example, the compound II was prepared in a multi-step synthesis. II showed antagonistic effect on Group II metabotropic glutamate receptor in rat. I are useful for the treatment of schizophrenia, anxiety, and diseases related to these, i.e., psychiatrical disorders such as depression, bipolar disorder, and epilepsy (no data).

IT 820244-11-9P 820244-46-0P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; preparation of 2-aminobicyclo[3.1.0]hexane-2,6-dicarboxylic acid esters as Group II metabotropic glutamate receptor antagonists)

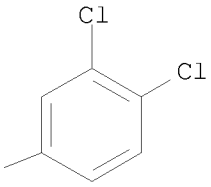
RN 820244-11-9 CAPLUS
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-3-[(3,4-dichlorophenyl)methoxy]-6-fluoro-, 6-[(2E,6E)-3,7,11-trimethyl-2,6,10-dodecatrien-1-yl] ester, (1R,2R,3R,5R,6R)- (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A

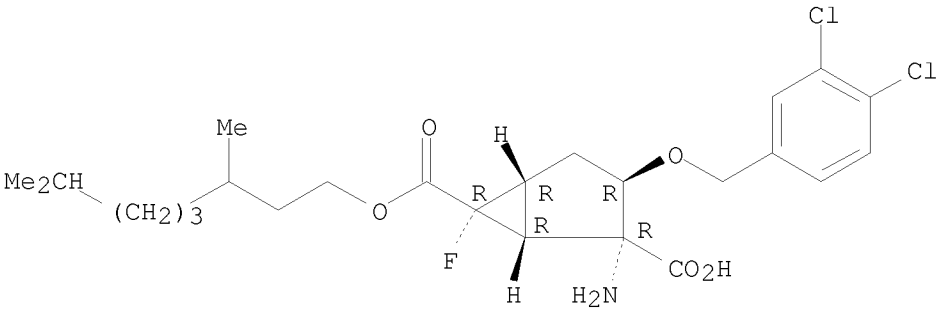


PAGE 1-B



RN 820244-46-0 CAPLUS
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-3-[(3,4-dichlorophenyl)methoxy]-6-fluoro-, 6-(3,7-dimethyloctyl) ester, (1R,2R,3R,5R,6R)- (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 3 OF 5 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2004:1038326 CAPLUS
DOCUMENT NUMBER: 142:16843
TITLE: mGluR2 antagonists and 2-amino-3-alkoxy-6-[3.1.0]hexan-2,6-dicarboxylate derivatives for treatment of nervous system diseases
INVENTOR(S): Nakazato, Atsuro; Taki, Shigeyuki; Sakagami, Kazunari; Dean, Reiko; Ota, Hiroyuki; Hirota, Shiho; Yasuhara, Akitaka
PATENT ASSIGNEE(S): Taisho Pharmaceutical Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 70 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2004339199	A	20041202	JP 2004-86153	20040324
PRIORITY APPLN. INFO.:			JP 2003-117907 A	20030423

OTHER SOURCE(S): MARPAT 142:16843
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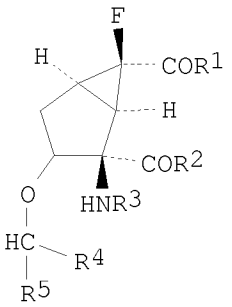


I

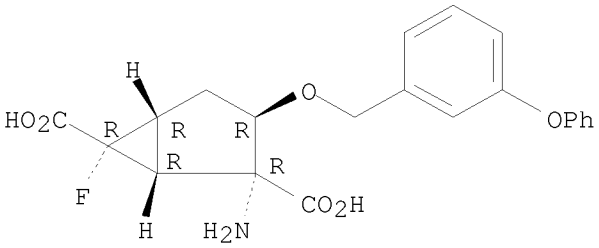
AB The antidepressant mGlur2 antagonists and

2-amino-3-alkoxy-6-[3.1.0]hexan-2,6-dicarboxylate derivs., salts, and hydrates are claimed for treatment of nervous system diseases, including bipolar affective disorder, psychiatry disorder, anxiety, epilepsy, drug dependence, cognition disorder, Alzheimer's disease, Huntington's disease, Parkinson disease, muscle stiffness, brain ischemia, spinal cord injury, head injury, etc.

IT 569686-67-5P 569686-89-1P 569686-92-6P
569687-04-3P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(6-Fluorobicyclo[3.1.0]hexane derivs. having group II metabotropic glutamate receptor antagonist actions as antidepressants)

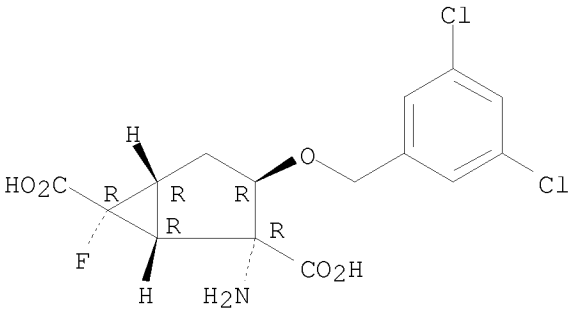
RN 569686-67-5 CAPLUS
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-6-fluoro-3-[(3-phenoxyphenyl)methoxy]-, (1R,2R,3R,5R,6R)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



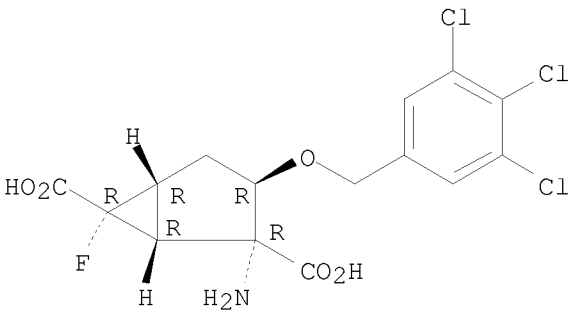
RN 569686-89-1 CAPLUS
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-3-[(3,5-dichlorophenyl)methoxy]-6-fluoro-, (1R,2R,3R,5R,6R)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



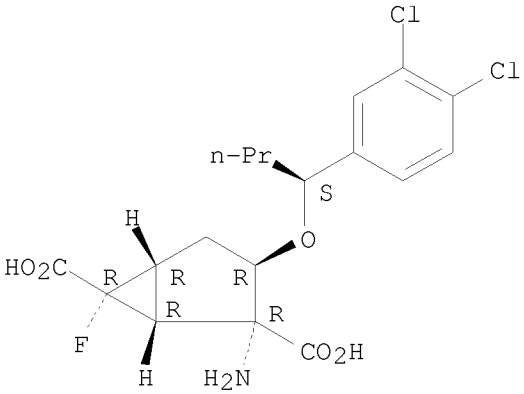
RN 569686-92-6 CAPLUS
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-6-fluoro-3-[(3,4,5-trichlorophenyl)methoxy]-, (1R,2R,3R,5R,6R)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



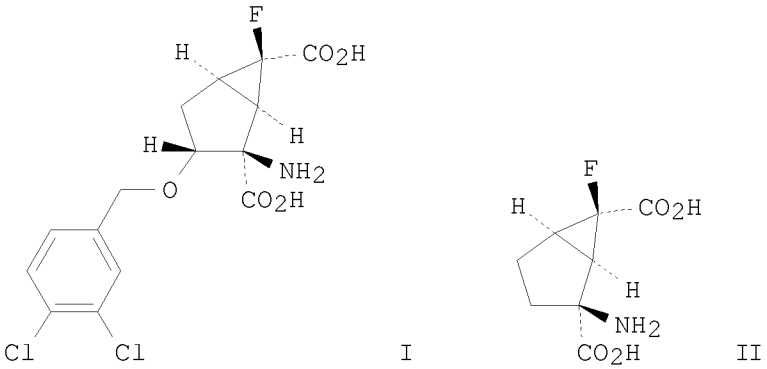
RN 569687-04-3 CAPLUS
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-3-[(1S)-1-(3,4-dichlorophenyl)butoxy]-6-fluoro-, (1R,2R,3R,5R,6R)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



L5 ANSWER 4 OF 5 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2004:620394 CAPLUS
DOCUMENT NUMBER: 141:243074
TITLE: Synthesis, in vitro pharmacology, structure-activity relationships, and pharmacokinetics of 3-alkoxy-2-amino-6-fluorobicyclo[3.1.0]hexane-2,6-dicarboxylic acid derivatives as potent and selective group II metabotropic glutamate receptor antagonists
AUTHOR(S): Nakazato, Atsuro; Sakagami, Kazunari; Yasuhara, Akito; Ohta, Hiroshi; Yoshikawa, Ryoko; Itoh, Manabu; Nakamura, Masato; Chaki, Shigeyuki
CORPORATE SOURCE: Medicinal Chemistry Laboratory, Taisho Pharmaceutical Co. Ltd., Kita-ku, Saitama-shi, Saitama, 331-9530, Japan
SOURCE: Journal of Medicinal Chemistry (2004), 47(18), 4570-4587
CODEN: JMCMAR; ISSN: 0022-2623

PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 141:243074
GI



AB Group II metabotropic glutamate receptor (mGluR) antagonists, 3-alkoxy-2-amino-6-fluorobicyclo[3.1.0]hexane-2,6-dicarboxylic acid derivs., e.g., I, were discovered by the incorporation of a hydroxy or alkoxyl group onto the C-3 portion of selective and potent group II mGluR agonist II. Among these compds., I (MGS0039) was a highly selective and potent group II mGluR antagonist with the best pharmacokinetic profile. I exhibited high affinities for mGlu 2 (Ki = 2.38 ± 0.40 nM) and mGlu 3 (4.46 ± 0.31 nM) but low affinity for mGluR 7 (Ki = 664 ± 106 nM), and potent antagonist activities for mGlu 2 (IC50 = 20.0 ± 3.67nM) and mGluR 3 (IC50 = 24.0 ± 3.54 nM) but much less potent antagonist activities for mGlu 4 (IC50 = 1740 ± 1080 nM), mGlu 6 (IC50 = 2060 ± 1270 nM), mGlu 1 (IC50 = 93300 ± 14600 nM), and mGluR 5 (IC50 = 117000 ± 38600 nM). No significant agonist activities of I were found for mGluRs 2, 3, 4, 6, 1, and 5 (EC50 > 100000 nM). Furthermore, I exhibited dose-dependent oral absorption (plasma Cmax: 214 ± 56.7, 932 ± 235, and 2960 ± 1150 ng/mL for 3 mg/kg, 10 mg/kg, and 30 mg/kg, po, resp.) and acceptable blood-brain barrier penetration (brain Cmax: 13.2 ng/mL for 10 mg/kg, po 6 h). The synthesis, in vitro pharmacol. profile, and structure-activity relationships of 3-alkoxy-2-amino-6-fluorobicyclo[3.1.0]hexane-2,6-dicarboxylic acid derivs., and pharmacokinetic profiles of several typical compds, are presented.

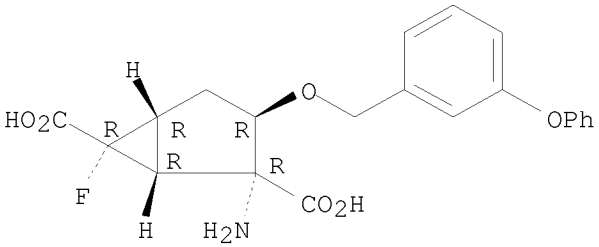
IT 569686-67-5P 569686-89-1P 569686-92-6P
569687-04-3P
RL: PAC (Pharmacological activity); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(preparation of alkoxy(amino)fluorobicyclohexanedicarboxylic acid derivs. and their binding affinity of group II metabotropic glutamate receptors and structure-activity relationship starting from chiral fluoro(oxo)bicyclohexanecarboxylates)

RN 569686-67-5 CAPLUS

CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-6-fluoro-3-[(3-phenoxyphenyl)methoxy]-, (1R,2R,3R,5R,6R)- (CA

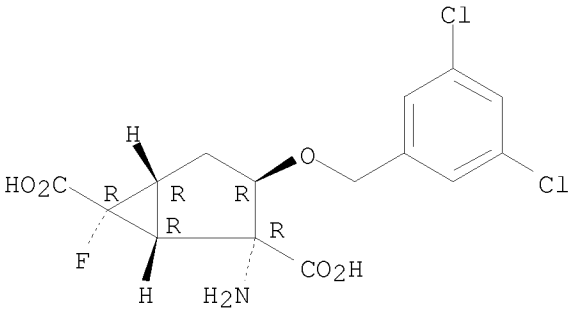
INDEX NAME)

Absolute stereochemistry. Rotation (-).



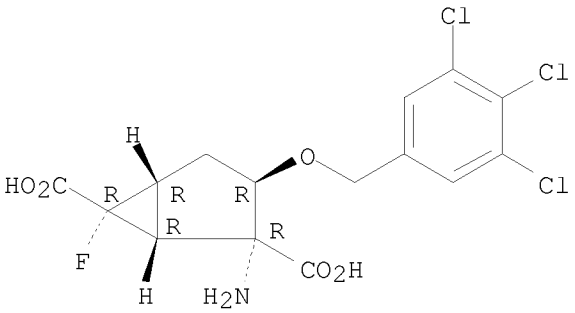
RN 569686-89-1 CAPLUS
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-3-[(3,5-dichlorophenyl)methoxy]-6-fluoro-, (1R,2R,3R,5R,6R)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RN 569686-92-6 CAPLUS
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-6-fluoro-3-[(3,4,5-trichlorophenyl)methoxy]-, (1R,2R,3R,5R,6R)- (CA INDEX NAME)

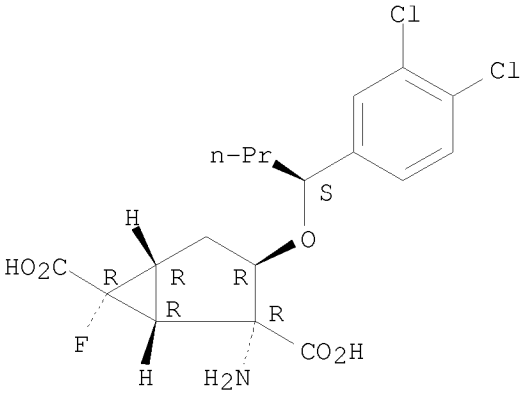
Absolute stereochemistry. Rotation (-).



RN 569687-04-3 CAPLUS

CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-3-[(1S)-1-(3,4-dichlorophenyl)butoxy]-6-fluoro-, (1R,2R,3R,5R,6R)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



OS.CITING REF COUNT: 18 THERE ARE 18 CAPLUS RECORDS THAT CITE THIS RECORD (18 CITINGS)
REFERENCE COUNT: 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 5 OF 5 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2003:591035 CAPLUS
DOCUMENT NUMBER: 139:143973
TITLE: 6-Fluorobicyclo[3.1.0]hexane derivatives
INVENTOR(S): Nakazato, Atsuro; Chaki, Shigeyuki; Sakagami, Kazunari; Dean, Ryoko; Ohta, Hiroshi; Hirota, Shiho; Yasuhara, Akito
PATENT ASSIGNEE(S): Taisho Pharmaceutical Co.,ltd., Japan
SOURCE: PCT Int. Appl., 98 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003061698	A1	20030731	WO 2002-JP13693	20021226
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
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EP 1459765	A1	20040922	EP 2002-793421		20021226
EP 1459765	B1	20080820			
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BR 2002015462	A	20041130	BR 2002-15462		20021226
CN 1610557	A	20050427	CN 2002-826388		20021226
CN 1281274	C	20061025			
ZA 2005002085	A	20050629	ZA 2005-2085		20021226
HU 2004002649	A2	20051028	HU 2004-2649		20021226
NZ 533699	A	20060526	NZ 2002-533699		20021226
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ES 2311642	T3	20090216	ES 2002-793421		20021226
JP 4230919	B2	20090225	JP 2003-561641		20021226
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IN 2004CN01417	A	20060210	IN 2004-CN1417		20040623
MX 2004006322	A	20041004	MX 2004-6322		20040625
KR 897970	B1	20090518	KR 2004-710069		20040625
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US 7157594	B2	20070102			
HK 1073258	A1	20070323	HK 2005-106035		20050715
KR 2009031962	A	20090330	KR 2009-705135		20090312
PRIORITY APPLN. INFO.:			JP 2001-395797	A	20011227
			WO 2002-JP13693	W	20021226
			KR 2004-710069	A3	20040625

OTHER SOURCE(S): MARPAT 139:143973

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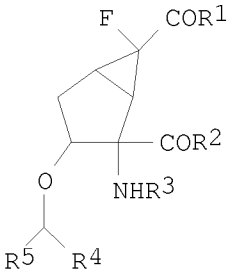


I

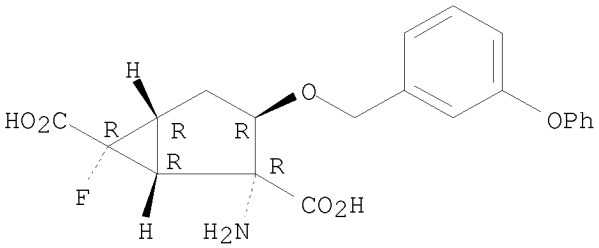
AB Antidepressants containing as the active ingredient compds. having group II metabotropic glutamate receptor antagonism; and 2-amino-3-alkoxy-6-fluorobicyclo[3.1.0]- hexane-2,6-dicarboxylic acid derivs. represented by the general formula [I], pharmaceutically acceptable salts thereof, or hydrates of the salts: I wherein R1 and R2 may be the same or different from each other and are each hydroxyl, C1-10 alkoxy, or the like; R3 is C1-10 acyl, C1-6 alkoxy-C1-6 acyl, or the like; and R4 and R5 may be the same or different from each other and are each hydrogen, C1-10 alkyl, or the like.

IT 569686-67-5P 569686-89-1P 569686-92-6P

569687-04-3P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(6-Fluorobicyclo[3.1.0]hexane derivs. having group II metabotropic glutamate receptor antagonist actions as antidepressants)

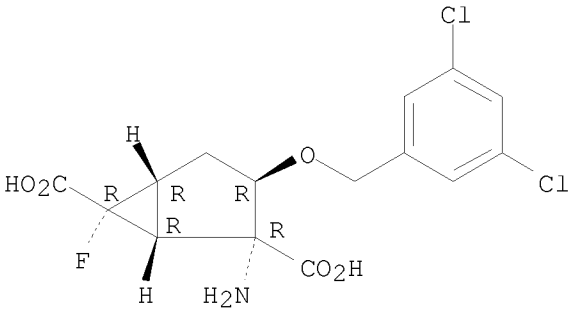
RN 569686-67-5 CAPLUS
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-6-fluoro-3-[(3-phenoxyphenyl)methoxy]-, (1R,2R,3R,5R,6R)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



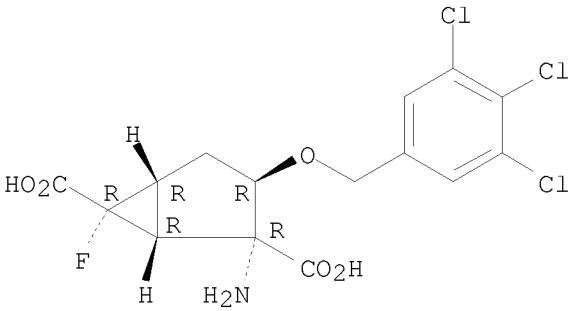
RN 569686-89-1 CAPLUS
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-3-[(3,5-dichlorophenyl)methoxy]-6-fluoro-, (1R,2R,3R,5R,6R)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



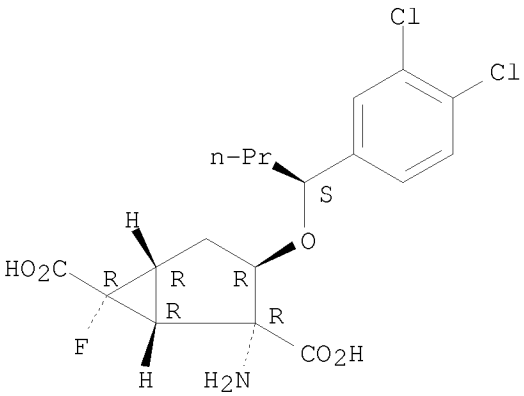
RN 569686-92-6 CAPLUS
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-6-fluoro-3-[(3,4,5-trichlorophenyl)methoxy]-, (1R,2R,3R,5R,6R)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RN 569687-04-3 CAPLUS
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid,
2-amino-3-[(1S)-1-(3,4-dichlorophenyl)butoxy]-6-fluoro-, (1R,2R,3R,5R,6R)-
(CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



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REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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Substance data SEARCH and crossover from CAS REGISTRY in progress...
Use DISPLAY HITSTR (or FHITSTR) to directly view retrieved structures.

THE ESTIMATED SEARCH COST FOR FILE 'REGISTRY' IS 185.40 U.S. DOLLARS
DO YOU WANT TO CONTINUE WITH THIS REQUEST? (Y)/N or END:y
FULL SEARCH INITIATED 16:17:19 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 328 TO ITERATE

100.0% PROCESSED 328 ITERATIONS 112 ANSWERS
SEARCH TIME: 00.00.01

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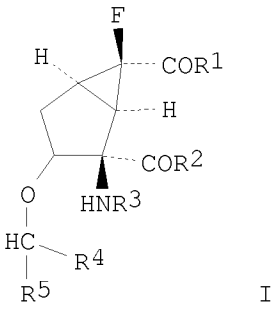
THE ESTIMATED COST FOR THIS REQUEST IS 33.84 U.S. DOLLARS
DO YOU WANT TO CONTINUE WITH THIS REQUEST? (Y)/N:y

L7 ANSWER 18 OF 23 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2004:1038326 CAPLUS
DOCUMENT NUMBER: 142:16843
TITLE: mGluR2 antagonists and 2-amino-3-alkoxy-6-[3.1.0]hexan-2,6-dicarboxylate derivatives for treatment of nervous system diseases
INVENTOR(S): Nakazato, Atsuro; Taki, Shigeyuki; Sakagami, Kazunari; Dean, Reiko; Ota, Hiroyuki; Hirota, Shiho; Yasuhara, Akitaka
PATENT ASSIGNEE(S): Taisho Pharmaceutical Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 70 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2004339199	A	20041202	JP 2004-86153	20040324
PRIORITY APPLN. INFO.:			JP 2003-117907 A	20030423

OTHER SOURCE(S): MARPAT 142:16843
GI



I

AB The antidepressant mGlur2 antagonists and 2-amino-3-alkoxy-6-[3.1.0]hexan-2,6-dicarboxylate derivs., salts, and hydrates are claimed for treatment of nervous system diseases, including bipolar affective disorder, psychiatry disorder, anxiety, epilepsy, drug dependence, cognition disorder, Alzheimer's disease, Huntington's disease, Parkinson disease, muscle stiffness, brain ischemia, spinal cord injury, head injury, etc.

IT 569686-59-5P 569686-61-9P 569686-62-0P
569686-63-1P 569686-64-2P 569686-65-3P
569686-66-4P 569686-67-5P 569686-68-6P
569686-69-7P 569686-70-0P 569686-71-1P
569686-72-2P 569686-73-3P 569686-74-4P
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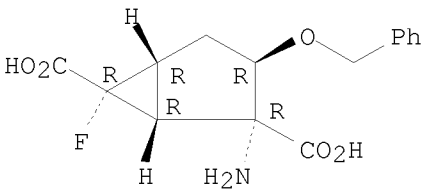
569687-10-1P 569687-11-2P 569687-13-4P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(6-Fluorobicyclo[3.1.0]hexane derivs. having group II metabotropic glutamate receptor antagonist actions as antidepressants)

RN 569686-59-5 CAPLUS

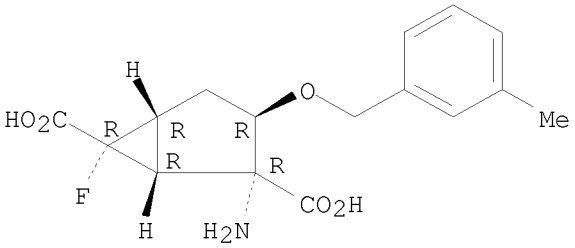
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-6-fluoro-3-(phenylmethoxy)-, (1R,2R,3R,5R,6R)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



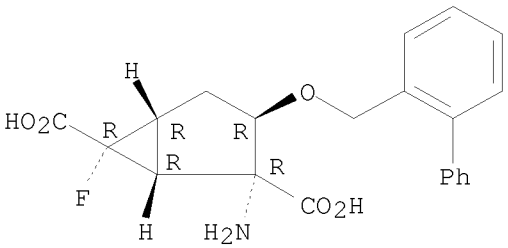
RN 569686-61-9 CAPLUS
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-6-fluoro-3-[(3-methylphenyl)methoxy]-, (1R,2R,3R,5R,6R)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



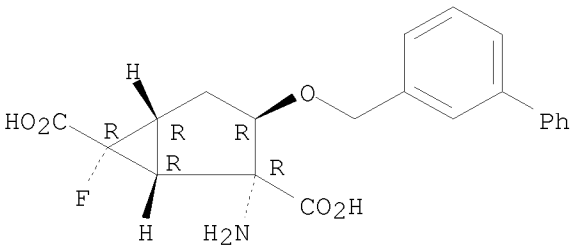
RN 569686-62-0 CAPLUS
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-3-([1,1'-biphenyl]-2-ylmethoxy)-6-fluoro-, (1R,2R,3R,5R,6R)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RN 569686-63-1 CAPLUS
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-3-([1,1'-biphenyl]-3-ylmethoxy)-6-fluoro-, (1R,2R,3R,5R,6R)- (CA INDEX NAME)

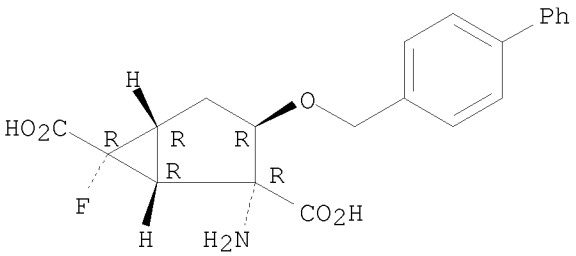
Absolute stereochemistry. Rotation (-).



RN 569686-64-2 CAPLUS
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid,

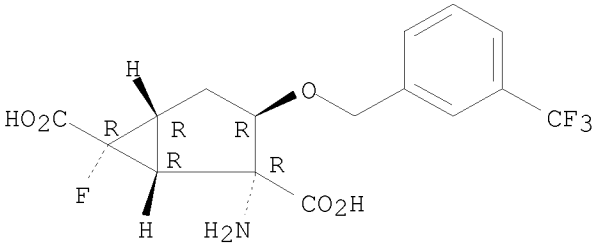
2-amino-3-([1,1'-biphenyl]-4-ylmethoxy)-6-fluoro-, (1R,2R,3R,5R,6R)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



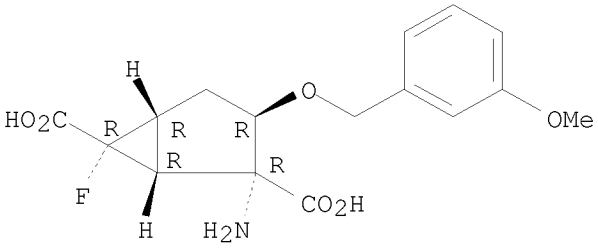
RN 569686-65-3 CAPLUS
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-6-fluoro-3-[[3-(trifluoromethyl)phenyl]methoxy]-, (1R,2R,3R,5R,6R)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



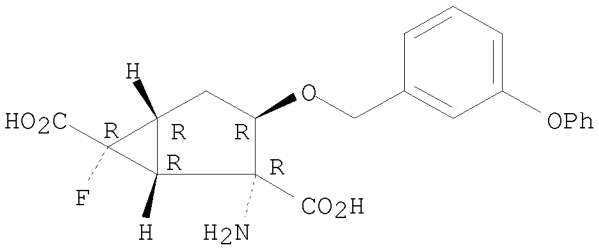
RN 569686-66-4 CAPLUS
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-6-fluoro-3-[(3-methoxyphenyl)methoxy]-, (1R,2R,3R,5R,6R)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



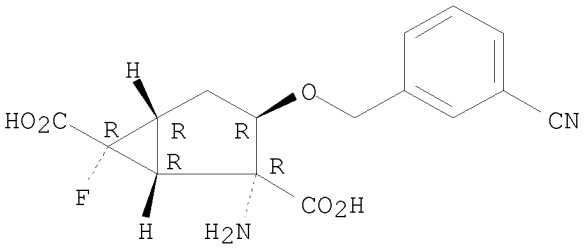
RN 569686-67-5 CAPLUS
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-6-fluoro-3-[(3-phenoxyphenyl)methoxy]-, (1R,2R,3R,5R,6R)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



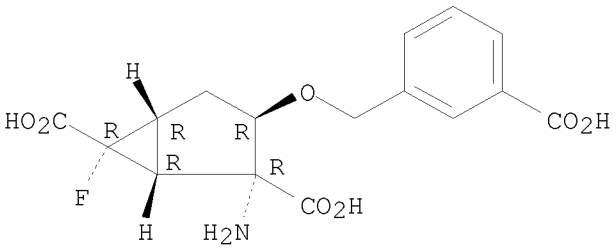
RN 569686-68-6 CAPLUS
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-3-[(3-cyanophenyl)methoxy]-6-fluoro-, (1R,2R,3R,5R,6R)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



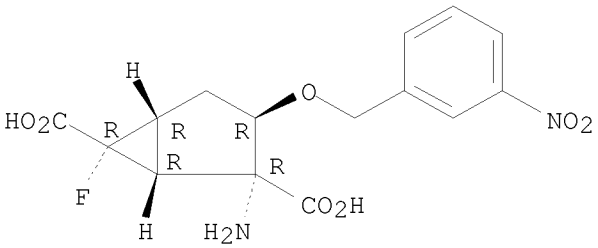
RN 569686-69-7 CAPLUS
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-3-[(3-carboxyphenyl)methoxy]-6-fluoro-, (1R,2R,3R,5R,6R)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



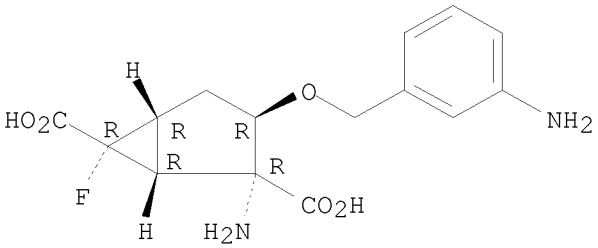
RN 569686-70-0 CAPLUS
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-6-fluoro-3-[(3-nitrophenyl)methoxy]-, (1R,2R,3R,5R,6R)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



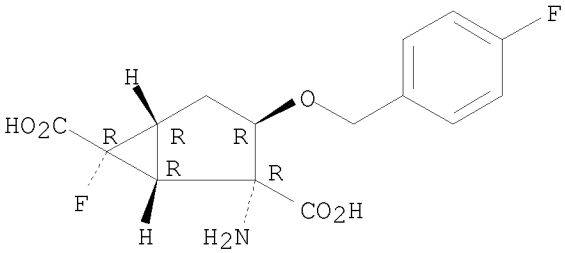
RN 569686-71-1 CAPLUS
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-3-[(3-aminophenyl)methoxy]-6-fluoro-, (1R,2R,3R,5R,6R)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



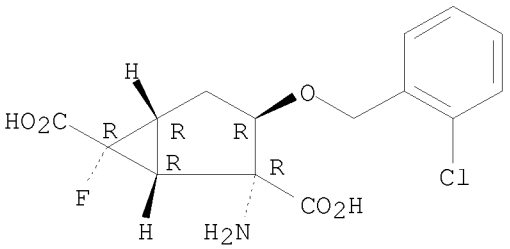
RN 569686-72-2 CAPLUS
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-6-fluoro-3-[(4-fluorophenyl)methoxy]-, (1R,2R,3R,5R,6R)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



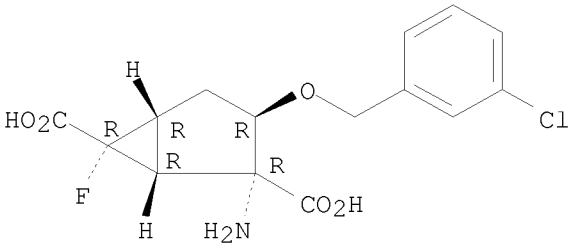
RN 569686-73-3 CAPLUS
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-3-[(2-chlorophenyl)methoxy]-6-fluoro-, (1R,2R,3R,5R,6R)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



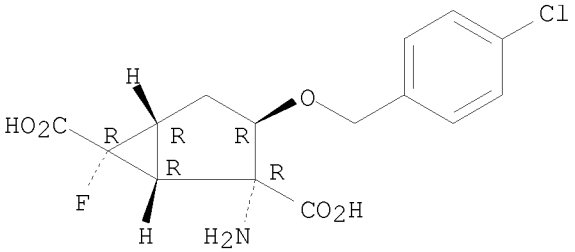
RN 569686-74-4 CAPLUS
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-3-[(3-chlorophenyl)methoxy]-6-fluoro-, (1R,2R,3R,5R,6R)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



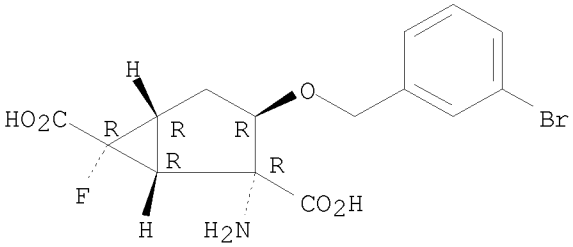
RN 569686-75-5 CAPLUS
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-3-[(4-chlorophenyl)methoxy]-6-fluoro-, (1R,2R,3R,5R,6R)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



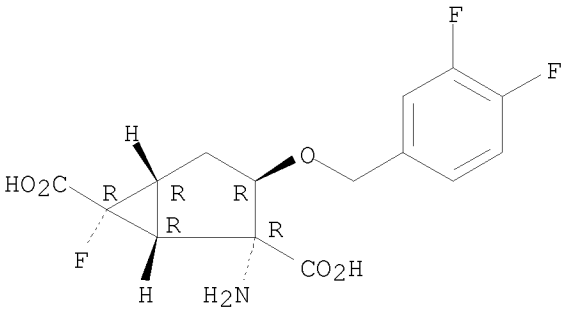
RN 569686-76-6 CAPLUS
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-3-[(3-bromophenyl)methoxy]-6-fluoro-, (1R,2R,3R,5R,6R)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



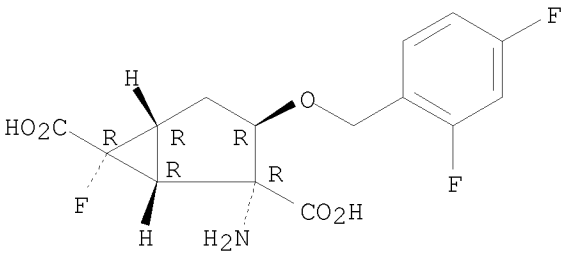
RN 569686-77-7 CAPLUS
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-3-[(3,4-difluorophenyl)methoxy]-6-fluoro-, (1R,2R,3R,5R,6R)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



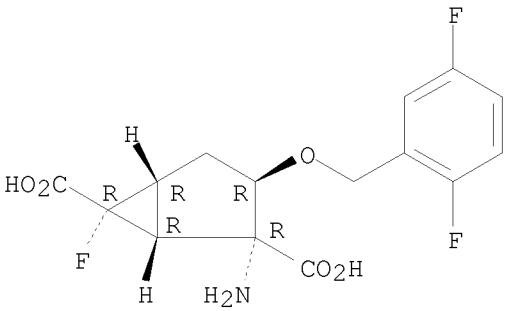
RN 569686-78-8 CAPLUS
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-3-[(2,4-difluorophenyl)methoxy]-6-fluoro-, (1R,2R,3R,5R,6R)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



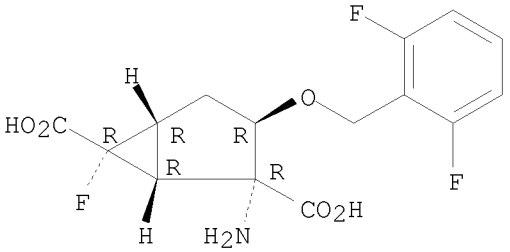
RN 569686-79-9 CAPLUS
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-3-[(2,5-difluorophenyl)methoxy]-6-fluoro-, (1R,2R,3R,5R,6R)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



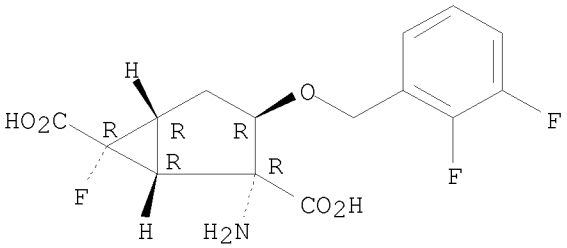
RN 569686-80-2 CAPLUS
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-3-[(2,6-difluorophenyl)methoxy]-6-fluoro-, (1R,2R,3R,5R,6R)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



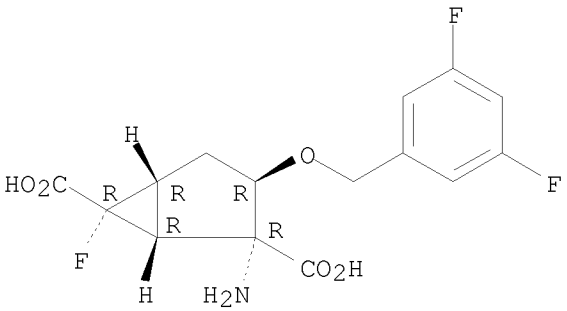
RN 569686-81-3 CAPLUS
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-3-[(2,3-difluorophenyl)methoxy]-6-fluoro-, (1R,2R,3R,5R,6R)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



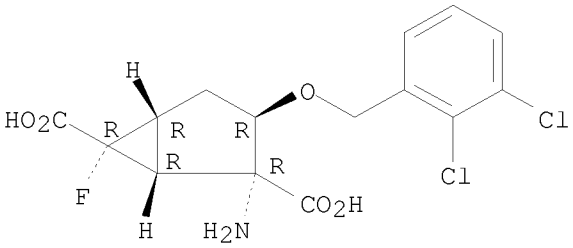
RN 569686-82-4 CAPLUS
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-3-[(3,5-difluorophenyl)methoxy]-6-fluoro-, (1R,2R,3R,5R,6R)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



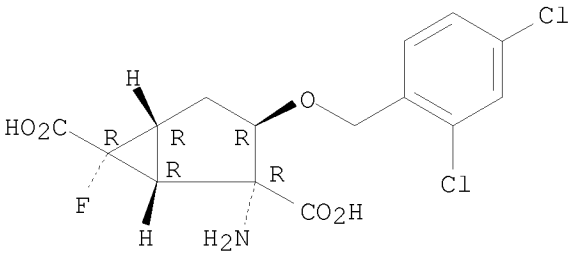
RN 569686-83-5 CAPLUS
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-3-[(2,3-dichlorophenyl)methoxy]-6-fluoro-, (1R,2R,3R,5R,6R)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



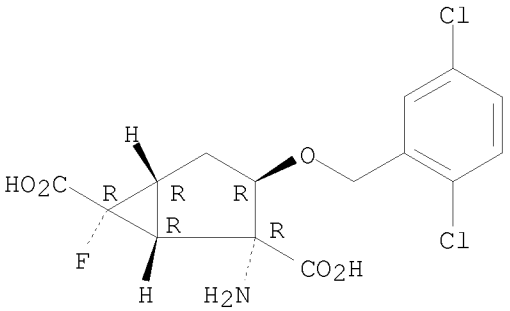
RN 569686-84-6 CAPLUS
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-3-[(2,4-dichlorophenyl)methoxy]-6-fluoro-, (1R,2R,3R,5R,6R)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



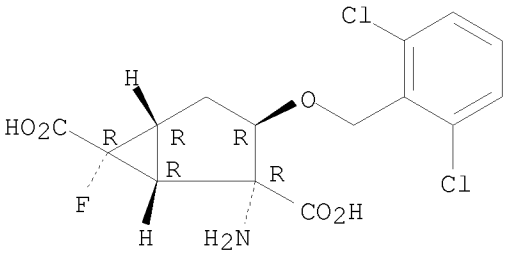
RN 569686-85-7 CAPLUS
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-3-[(2,5-dichlorophenyl)methoxy]-6-fluoro-, (1R,2R,3R,5R,6R)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



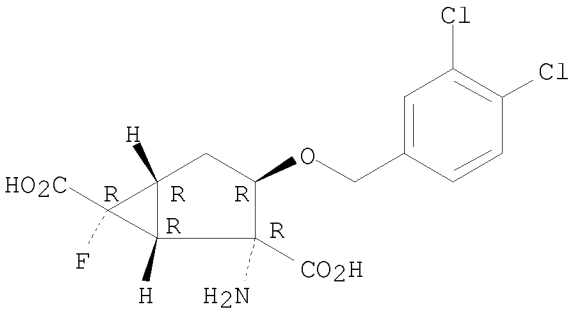
RN 569686-86-8 CAPLUS
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-3-[(2,6-dichlorophenyl)methoxy]-6-fluoro-, (1R,2R,3R,5R,6R)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



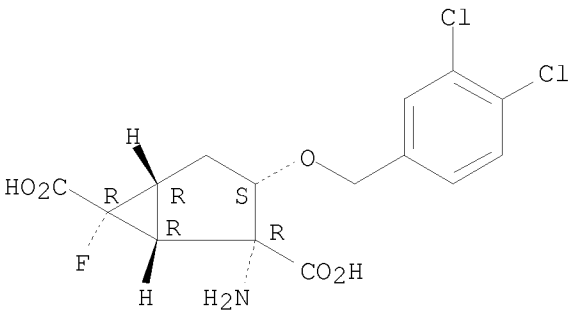
RN 569686-87-9 CAPLUS
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-3-[(3,4-dichlorophenyl)methoxy]-6-fluoro-, (1R,2R,3R,5R,6R)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



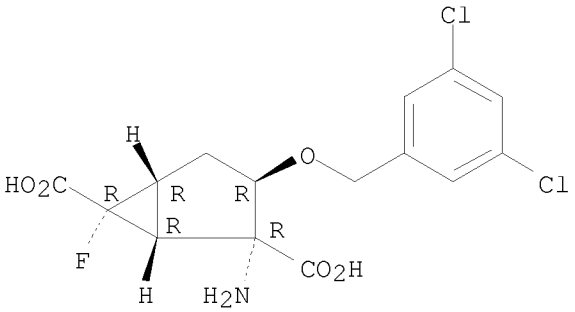
RN 569686-88-0 CAPLUS
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-3-[(3,4-dichlorophenyl)methoxy]-6-fluoro-, (1R,2R,3S,5R,6R)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



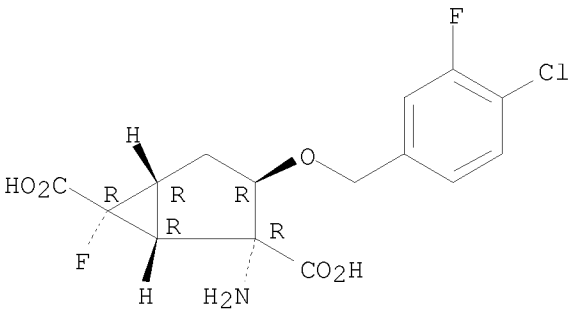
RN 569686-89-1 CAPLUS
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-3-[(3,5-dichlorophenyl)methoxy]-6-fluoro-, (1R,2R,3R,5R,6R)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RN 569686-90-4 CAPLUS
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-3-[(4-chloro-3-fluorophenyl)methoxy]-6-fluoro-, (1R,2R,3R,5R,6R)- (CA INDEX NAME)

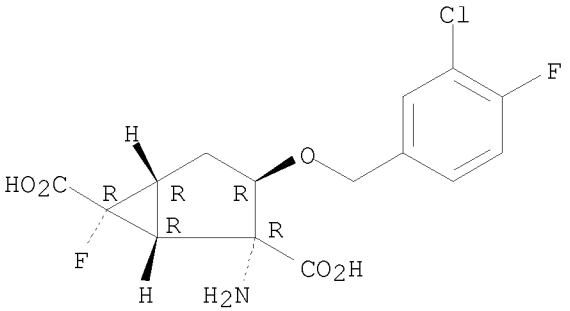
Absolute stereochemistry. Rotation (-).



RN 569686-91-5 CAPLUS

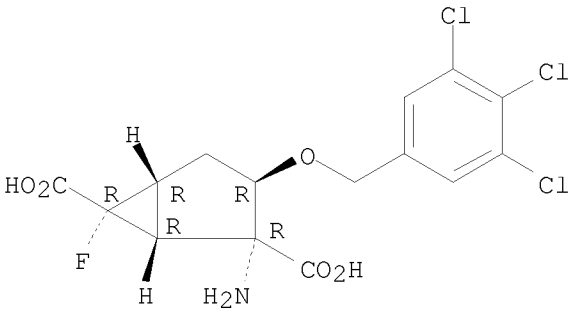
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid,
2-amino-3-[(3-chloro-4-fluorophenyl)methoxy]-6-fluoro-, (1R,2R,3R,5R,6R)-
(CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



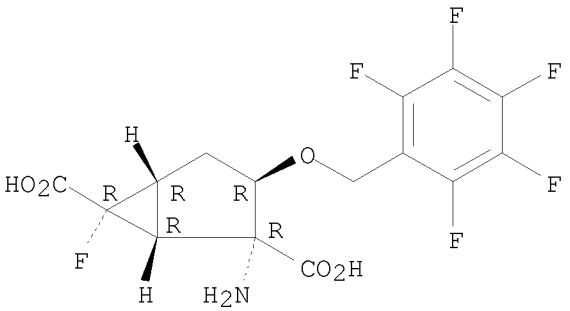
RN 569686-92-6 CAPLUS
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid,
2-amino-6-fluoro-3-[(3,4,5-trichlorophenyl)methoxy]-, (1R,2R,3R,5R,6R)-
(CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

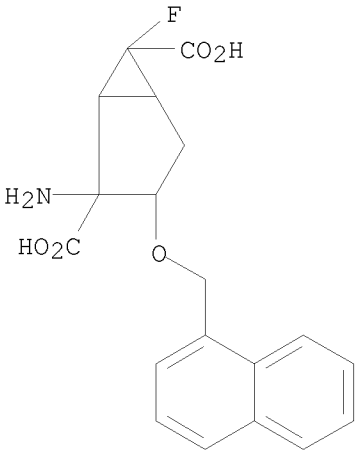


RN 569686-93-7 CAPLUS
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid,
2-amino-6-fluoro-3-[(2,3,4,5,6-pentafluorophenyl)methoxy]-,
(1R,2R,3R,5R,6R)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

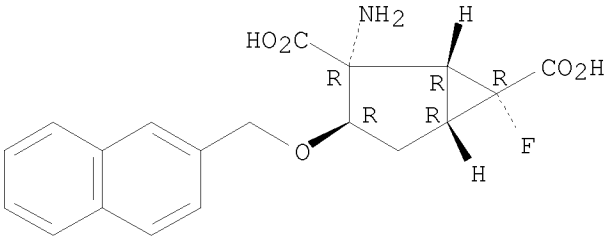


RN 569686-94-8 CAPLUS
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-6-fluoro-3-(1-naphthalenylmethoxy)-, (1R,2R,3R,5R,6R)- (CA INDEX NAME)



RN 569686-95-9 CAPLUS
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-6-fluoro-3-(2-naphthalenylmethoxy)-, (1R,2R,3R,5R,6R)- (CA INDEX NAME)

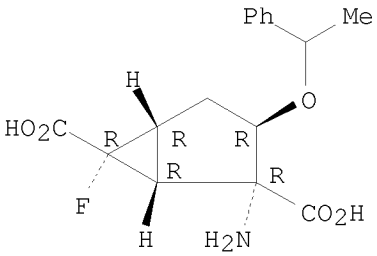
Absolute stereochemistry. Rotation (+).



RN 569686-98-2 CAPLUS

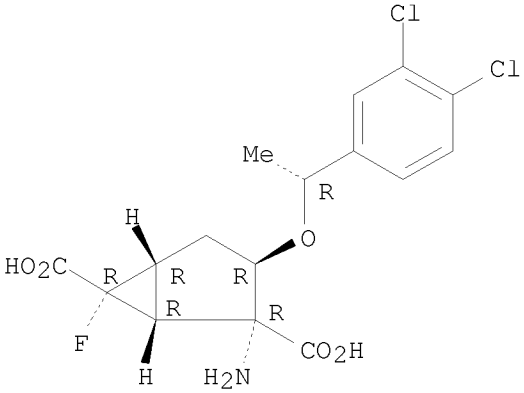
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid,
2-amino-6-fluoro-3-(1-phenylethoxy)-, (1R,2R,3R,5R,6R)- (CA INDEX NAME)

Absolute stereochemistry.



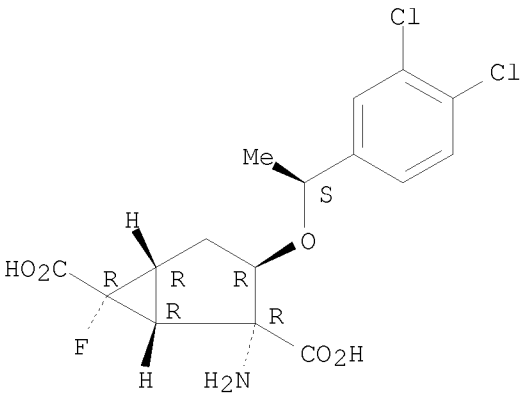
RN 569686-99-3 CAPLUS
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid,
2-amino-3-[(1R)-1-(3,4-dichlorophenyl)ethoxy]-6-fluoro-, (1R,2R,3R,5R,6R)-
(CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



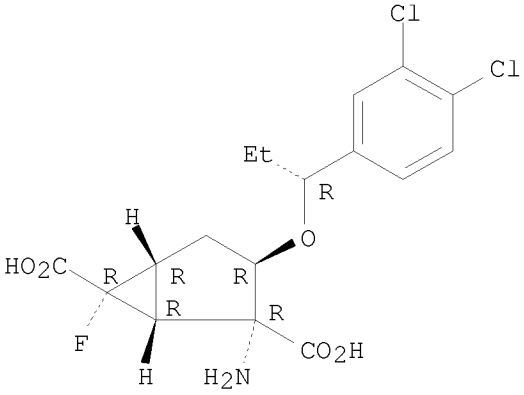
RN 569687-00-9 CAPLUS
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid,
2-amino-3-[(1S)-1-(3,4-dichlorophenyl)ethoxy]-6-fluoro-, (1R,2R,3R,5R,6R)-
(CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



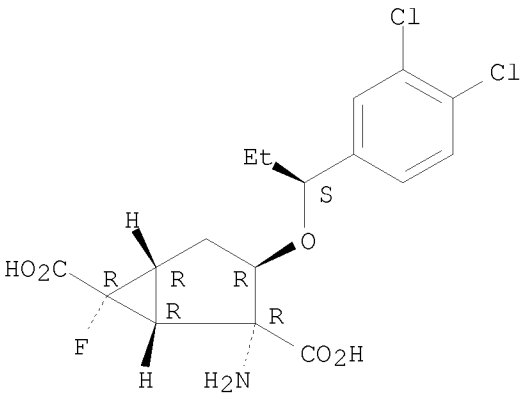
RN 569687-01-0 CAPLUS
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid,
2-amino-3-[(1R)-1-(3,4-dichlorophenyl)propoxy]-6-fluoro-,
(1R,2R,3R,5R,6R)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



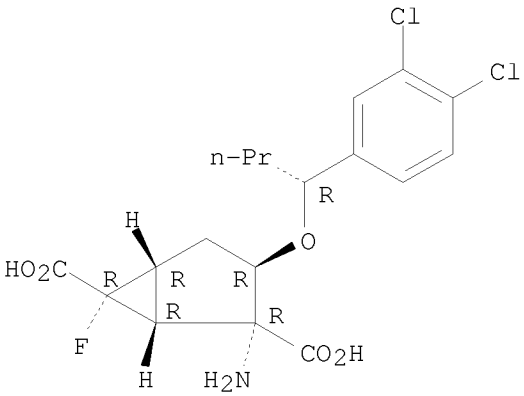
RN 569687-02-1 CAPLUS
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid,
2-amino-3-[(1S)-1-(3,4-dichlorophenyl)propoxy]-6-fluoro-,
(1R,2R,3R,5R,6R)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



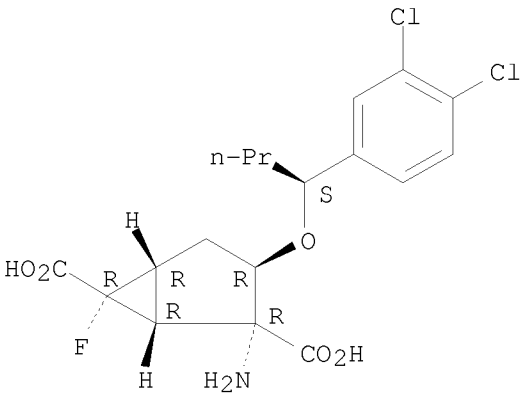
RN 569687-03-2 CAPLUS
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid,
2-amino-3-[(1R)-1-(3,4-dichlorophenyl)butoxy]-6-fluoro-, (1R,2R,3R,5R,6R)-
(CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



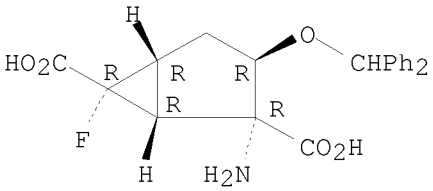
RN 569687-04-3 CAPLUS
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid,
2-amino-3-[(1S)-1-(3,4-dichlorophenyl)butoxy]-6-fluoro-, (1R,2R,3R,5R,6R)-
(CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



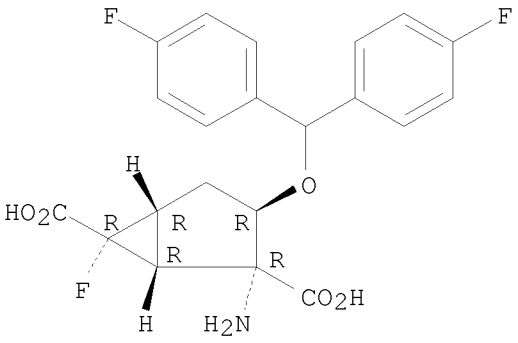
RN 569687-05-4 CAPLUS
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-3-(diphenylmethoxy)-6-fluoro-, (1R,2R,3R,5R,6R)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



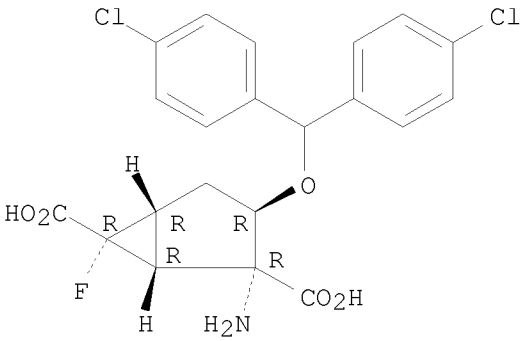
RN 569687-06-5 CAPLUS
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-3-[bis(4-fluorophenyl)methoxy]-6-fluoro-, (1R,2R,3R,5R,6R)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



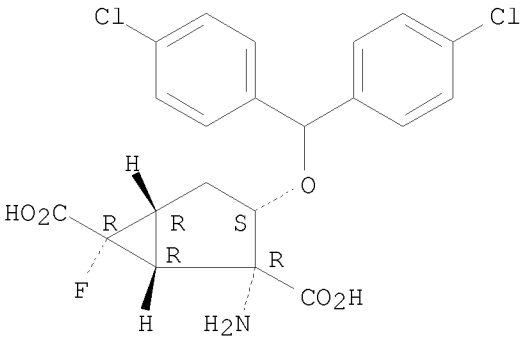
RN 569687-07-6 CAPLUS
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-3-[bis(4-chlorophenyl)methoxy]-6-fluoro-, (1R,2R,3R,5R,6R)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



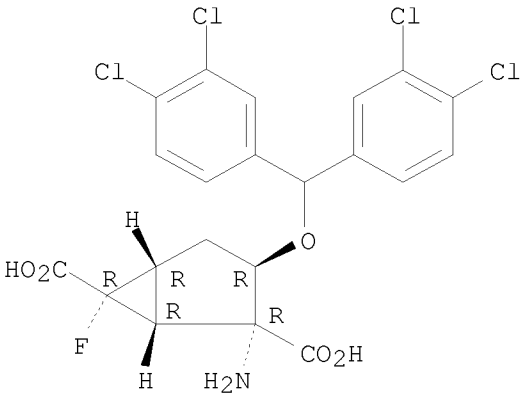
RN 569687-08-7 CAPLUS
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-3-[bis(4-chlorophenyl)methoxy]-6-fluoro-, (1R,2R,3S,5R,6R)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



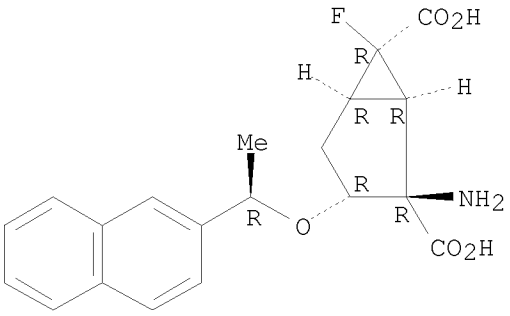
RN 569687-09-8 CAPLUS
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-3-[bis(3,4-dichlorophenyl)methoxy]-6-fluoro-, (1R,2R,3R,5R,6R)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



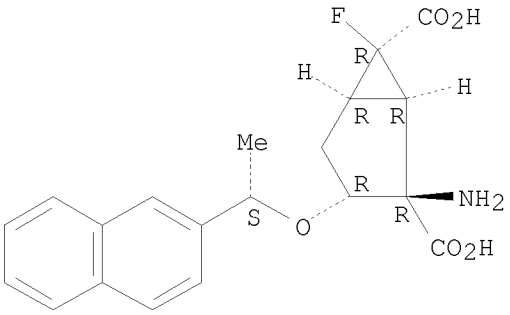
RN 569687-10-1 CAPLUS
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-6-fluoro-3-[(1R)-1-(2-naphthalenyl)ethoxy]-, (1R,2R,3R,5R,6R)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



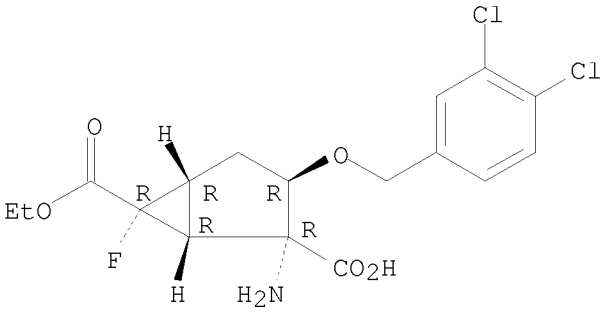
RN 569687-11-2 CAPLUS
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-6-fluoro-3-[(1S)-1-(2-naphthalenyl)ethoxy]-, (1R,2R,3R,5R,6R)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RN 569687-13-4 CAPLUS
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-3-[(3,4-dichlorophenyl)methoxy]-6-fluoro-, 6-ethyl ester, (1R,2R,3R,5R,6R)- (CA INDEX NAME)

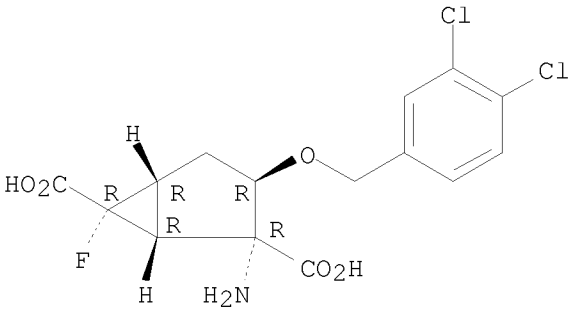
Absolute stereochemistry. Rotation (-).



L7 ANSWER 19 OF 23 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2004:814656 CAPLUS
DOCUMENT NUMBER: 141:325597
TITLE: Anxiolytic-like activity of MGS0039, a potent group II metabotropic glutamate receptor antagonist, in a marble-burying behavior test
AUTHOR(S): Shimazaki, Toshiharu; Iijima, Michihiko; Chaki, Shigeyuki
CORPORATE SOURCE: Psychiatric Diseases and Pain Research, Medicinal Pharmacology Laboratory, Medicinal Research Laboratories, Taisho Pharmaceutical Co., Ltd., Saitama, Saitama, 331-9530, Japan
SOURCE: European Journal of Pharmacology (2004), 501(1-3), 121-125
CODEN: EJPHAZ; ISSN: 0014-2999
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Glutamatergic abnormalities are involved in several psychiatric disorders. Clin. evidence demonstrates altered glutamatergic neurotransmission in patients suffering from obsessive-compulsive disorder. MGS0039, (1R,2R,3R,5R,6R)-2-amino-3-(3,4-dichlorobenzyloxy)-6-fluorobicyclo[3.1.0]hexane-2,6-dicarboxylic acid, is a novel group II metabotropic glutamate (mGlu) receptor antagonist. We examined MGS0039's potential anti-obsessive-compulsive disorder activity, using the marble-burying behavior test as a model of obsessive-compulsive disorder. MGS0039 as well as LY341495 ((2S,1'S,2'S)-2-(9-xanthylmethyl)-2-(2'-carboxycycloprolyl)glycine), another group II mGlu receptor antagonist, inhibited marble-burying behavior. We also demonstrated that this effect was significantly attenuated by a group II mGlu receptor agonist. This data indicates that group II mGlu receptor antagonists may exert anti-obsessive-compulsive disorder effects in clin. use.
IT 569686-87-9, MGS0039
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

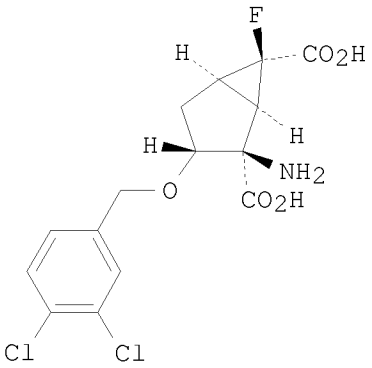
(anxiolytic-like activity of MGS0039, a potent group II metabotropic glutamate receptor antagonist, in a marble-burying behavior test)
RN 569686-87-9 CAPLUS
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-3-[(3,4-dichlorophenyl)methoxy]-6-fluoro-, (1R,2R,3R,5R,6R)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

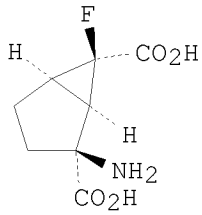


OS.CITING REF COUNT: 20 THERE ARE 20 CAPLUS RECORDS THAT CITE THIS RECORD (20 CITINGS)
REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 20 OF 23 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2004:620394 CAPLUS
DOCUMENT NUMBER: 141:243074
TITLE: Synthesis, in vitro pharmacology, structure-activity relationships, and pharmacokinetics of 3-alkoxy-2-amino-6-fluorobicyclo[3.1.0]hexane-2,6-dicarboxylic acid derivatives as potent and selective group II metabotropic glutamate receptor antagonists
AUTHOR(S): Nakazato, Atsuro; Sakagami, Kazunari; Yasuhara, Akito; Ohta, Hiroshi; Yoshikawa, Ryoko; Itoh, Manabu; Nakamura, Masato; Chaki, Shigeyuki
CORPORATE SOURCE: Medicinal Chemistry Laboratory, Taisho Pharmaceutical Co. Ltd., Kita-ku, Saitama-shi, Saitama, 331-9530, Japan
SOURCE: Journal of Medicinal Chemistry (2004), 47(18), 4570-4587
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 141:243074
GI



I



II

AB Group II metabotropic glutamate receptor (mGluR) antagonists, 3-alkoxy-2-amino-6-fluorobicyclo[3.1.0]hexane-2,6-dicarboxylic acid derivs., e.g., I, were discovered by the incorporation of a hydroxy or alkoxyl group onto the C-3 portion of selective and potent group II mGluR agonist II. Among these compds., I (MGS0039) was a highly selective and potent group II mGluR antagonist with the best pharmacokinetic profile. I exhibited high affinities for mGlu 2 (Ki = 2.38 ± 0.40 nM) and mGlu 3 (4.46 ± 0.31 nM) but low affinity for mGluR 7 (Ki = 664 ± 106 nM), and potent antagonist activities for mGlu 2 (IC50 = 20.0 ± 3.67nM) and mGluR 3 (IC50 = 24.0 ± 3.54 nM) but much less potent antagonist activities for mGlu 4 (IC50 = 1740 ± 1080 nM), mGlu 6 (IC50 = 2060 ± 1270 nM), mGlu 1 (IC50 = 93300 ± 14600 nM), and mGluR 5 (IC50 = 117000 ± 38600 nM). No significant agonist activities of I were found for mGluRs 2, 3, 4, 6, 1, and 5 (EC50 > 100000 nM). Furthermore, I exhibited dose-dependent oral absorption (plasma Cmax: 214 ± 56.7, 932 ± 235, and 2960 ± 1150 ng/mL for 3 mg/kg, 10 mg/kg, and 30 mg/kg, po, resp.) and acceptable blood-brain barrier penetration (brain Cmax: 13.2 ng/mL for 10 mg/kg, po 6 h). The synthesis, in vitro pharmacol. profile, and structure-activity relationships of 3-alkoxy-2-amino-6-fluorobicyclo[3.1.0]hexane-2,6-dicarboxylic acid derivs., and pharmacokinetic profiles of several typical compds, are presented.

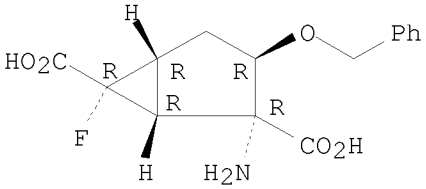
IT 569686-59-5P 569686-61-9P 569686-62-0P
569686-63-1P 569686-64-2P 569686-65-3P
569686-66-4P 569686-67-5P 569686-68-6P
569686-69-7P 569686-70-0P 569686-71-1P
569686-72-2P 569686-73-3P 569686-74-4P
569686-75-5P 569686-76-6P 569686-78-8P
569686-79-9P 569686-80-2P 569686-81-3P
569686-82-4P 569686-83-5P 569686-84-6P
569686-85-7P 569686-86-8P 569686-88-0P
569686-89-1P 569686-90-4P 569686-91-5P
569686-92-6P 569686-93-7P 569686-94-8P
569686-99-3P 569687-00-9P 569687-01-0P
569687-02-1P 569687-03-2P 569687-04-3P
569687-06-5P 569687-07-6P 569687-08-7P
569687-09-8P 569687-10-1P 569687-11-2P
748780-99-6P
RL: PAC (Pharmacological activity); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)

(preparation of alkoxy(amino)fluorobicyclohexanedicarboxylic acid derivs. and their binding affinity of group II metabotropic glutamate receptors and structure-activity relationship starting from chiral fluoro(oxo)bicyclohexanecarboxylates)

RN 569686-59-5 CAPLUS

CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-6-fluoro-3-(phenylmethoxy)-, (1R,2R,3R,5R,6R)- (CA INDEX NAME)

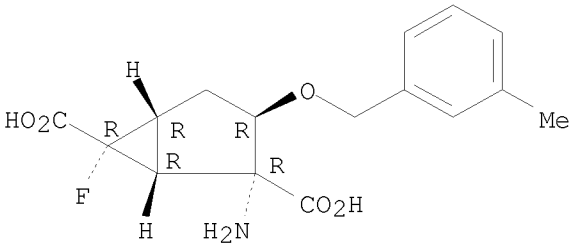
Absolute stereochemistry. Rotation (-).



RN 569686-61-9 CAPLUS

CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-6-fluoro-3-[(3-methylphenyl)methoxy]-, (1R,2R,3R,5R,6R)- (CA INDEX NAME)

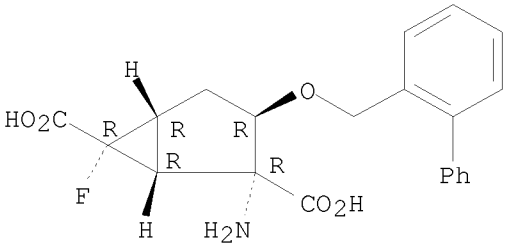
Absolute stereochemistry. Rotation (-).



RN 569686-62-0 CAPLUS

CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-3-([1,1'-biphenyl]-2-ylmethoxy)-6-fluoro-, (1R,2R,3R,5R,6R)- (CA INDEX NAME)

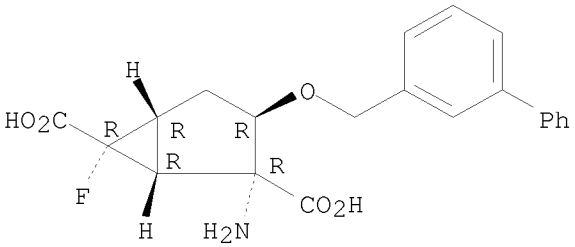
Absolute stereochemistry. Rotation (-).



RN 569686-63-1 CAPLUS

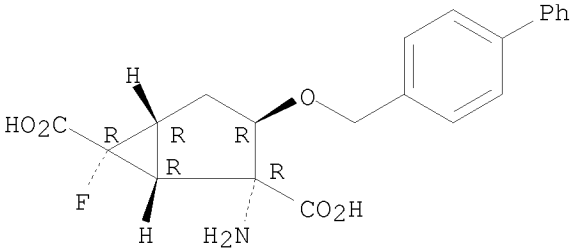
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-3-([1,1'-biphenyl]-3-ylmethoxy)-6-fluoro-, (1R,2R,3R,5R,6R)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



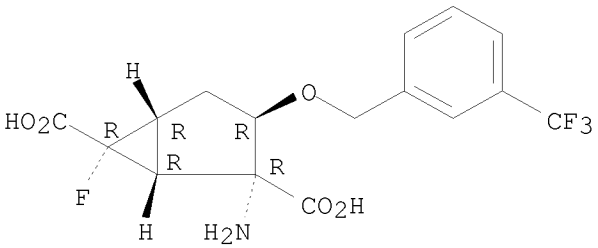
RN 569686-64-2 CAPLUS
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-3-([1,1'-biphenyl]-4-ylmethoxy)-6-fluoro-, (1R,2R,3R,5R,6R)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



RN 569686-65-3 CAPLUS
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-6-fluoro-3-[[3-(trifluoromethyl)phenyl]methoxy]-, (1R,2R,3R,5R,6R)- (CA INDEX NAME)

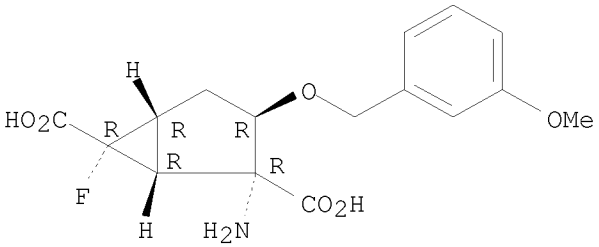
Absolute stereochemistry. Rotation (-).



RN 569686-66-4 CAPLUS
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-6-fluoro-3-[(3-methoxyphenyl)methoxy]-, (1R,2R,3R,5R,6R)- (CA

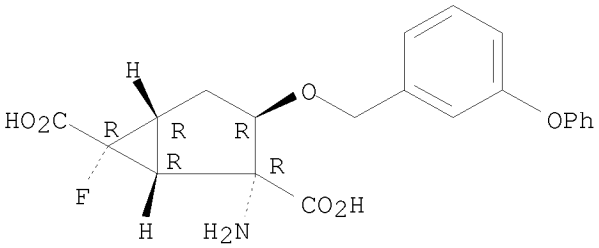
INDEX NAME)

Absolute stereochemistry. Rotation (-).



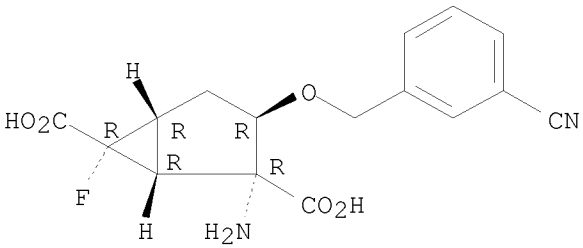
RN 569686-67-5 CAPLUS
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-6-fluoro-3-[(3-phenoxyphenyl)methoxy]-, (1R,2R,3R,5R,6R)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



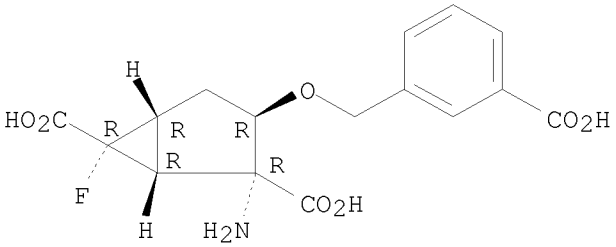
RN 569686-68-6 CAPLUS
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-3-[(3-cyanophenyl)methoxy]-6-fluoro-, (1R,2R,3R,5R,6R)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



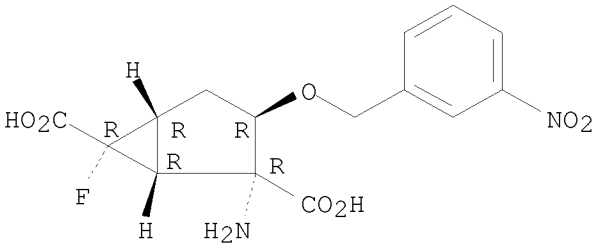
RN 569686-69-7 CAPLUS
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-3-[(3-carboxyphenyl)methoxy]-6-fluoro-, (1R,2R,3R,5R,6R)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



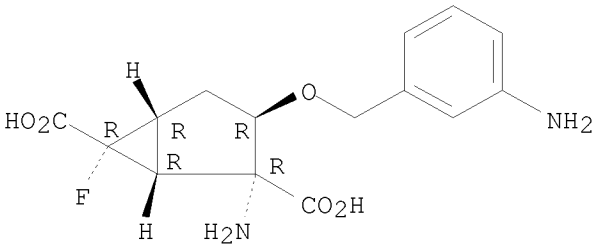
RN 569686-70-0 CAPLUS
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-6-fluoro-3-[(3-nitrophenyl)methoxy]-, (1R,2R,3R,5R,6R)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



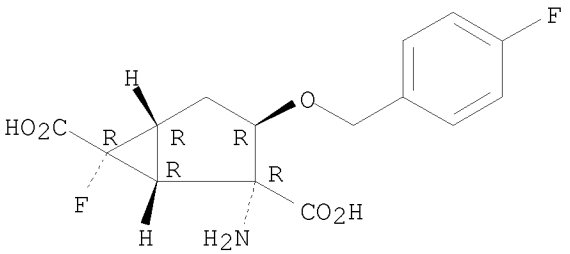
RN 569686-71-1 CAPLUS
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-3-[(3-aminophenyl)methoxy]-6-fluoro-, (1R,2R,3R,5R,6R)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



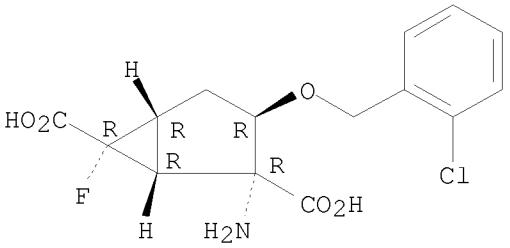
RN 569686-72-2 CAPLUS
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-6-fluoro-3-[(4-fluorophenyl)methoxy]-, (1R,2R,3R,5R,6R)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



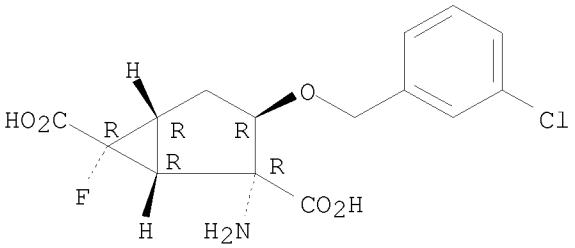
RN 569686-73-3 CAPLUS
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-3-[(2-chlorophenyl)methoxy]-6-fluoro-, (1R,2R,3R,5R,6R)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



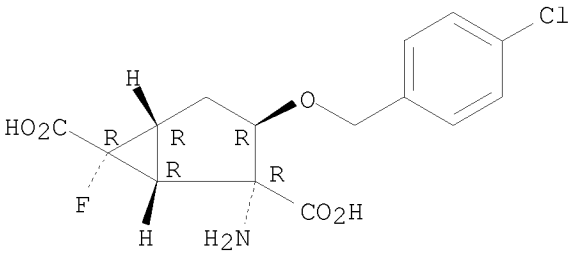
RN 569686-74-4 CAPLUS
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-3-[(3-chlorophenyl)methoxy]-6-fluoro-, (1R,2R,3R,5R,6R)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



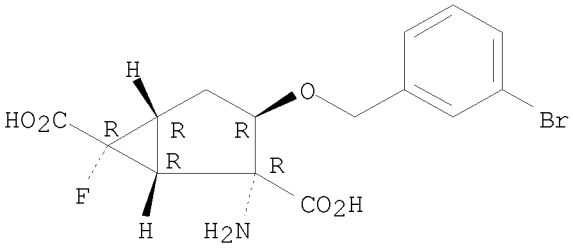
RN 569686-75-5 CAPLUS
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-3-[(4-chlorophenyl)methoxy]-6-fluoro-, (1R,2R,3R,5R,6R)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



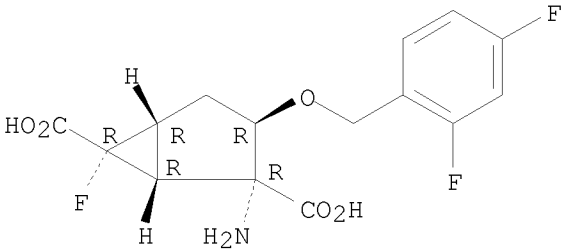
RN 569686-76-6 CAPLUS
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-3-[(3-bromophenyl)methoxy]-6-fluoro-, (1R,2R,3R,5R,6R)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



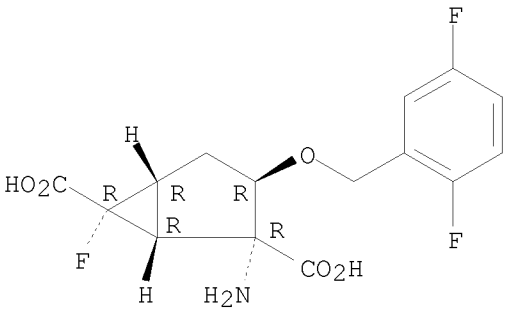
RN 569686-78-8 CAPLUS
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-3-[(2,4-difluorophenyl)methoxy]-6-fluoro-, (1R,2R,3R,5R,6R)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



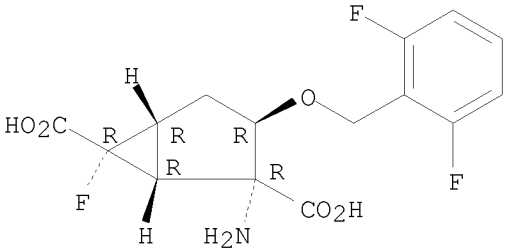
RN 569686-79-9 CAPLUS
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-3-[(2,5-difluorophenyl)methoxy]-6-fluoro-, (1R,2R,3R,5R,6R)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



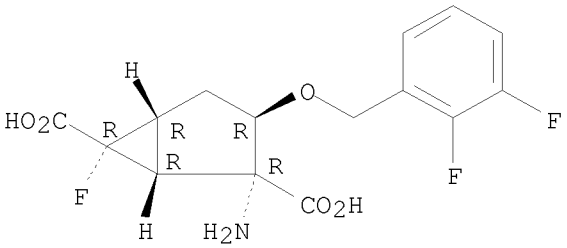
RN 569686-80-2 CAPLUS
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-3-[(2,6-difluorophenyl)methoxy]-6-fluoro-, (1R,2R,3R,5R,6R)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



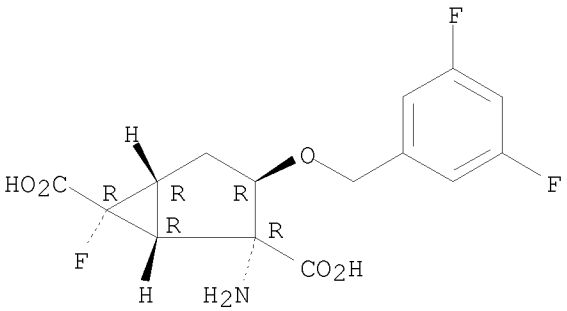
RN 569686-81-3 CAPLUS
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-3-[(2,3-difluorophenyl)methoxy]-6-fluoro-, (1R,2R,3R,5R,6R)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



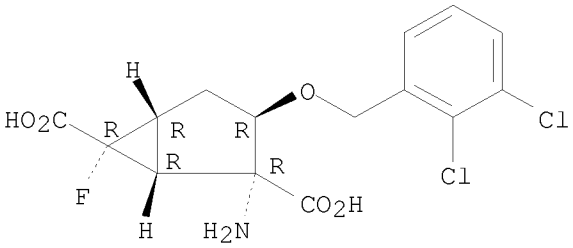
RN 569686-82-4 CAPLUS
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-3-[(3,5-difluorophenyl)methoxy]-6-fluoro-, (1R,2R,3R,5R,6R)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



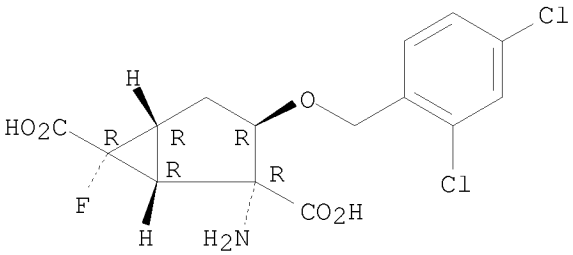
RN 569686-83-5 CAPLUS
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-3-[(2,3-dichlorophenyl)methoxy]-6-fluoro-, (1R,2R,3R,5R,6R)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



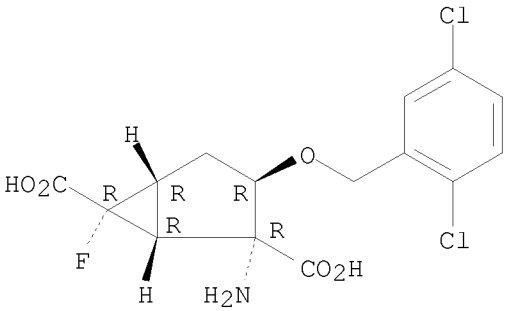
RN 569686-84-6 CAPLUS
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-3-[(2,4-dichlorophenyl)methoxy]-6-fluoro-, (1R,2R,3R,5R,6R)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



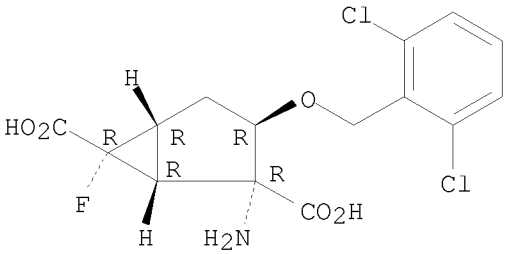
RN 569686-85-7 CAPLUS
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-3-[(2,5-dichlorophenyl)methoxy]-6-fluoro-, (1R,2R,3R,5R,6R)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



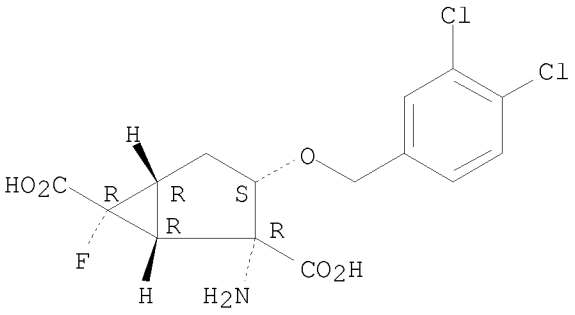
RN 569686-86-8 CAPLUS
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-3-[(2,6-dichlorophenyl)methoxy]-6-fluoro-, (1R,2R,3R,5R,6R)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



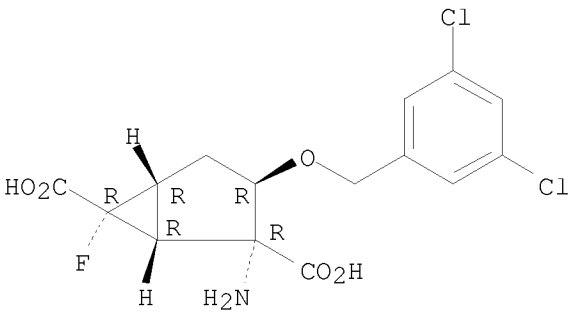
RN 569686-88-0 CAPLUS
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-3-[(3,4-dichlorophenyl)methoxy]-6-fluoro-, (1R,2R,3S,5R,6R)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



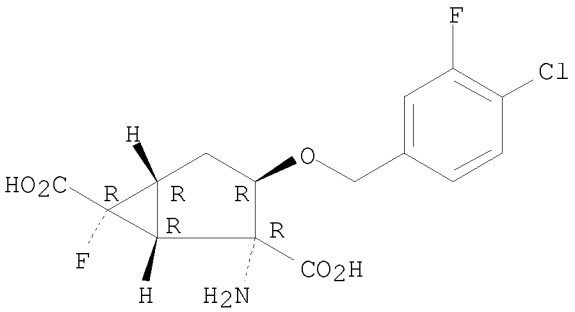
RN 569686-89-1 CAPLUS
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-3-[(3,5-dichlorophenyl)methoxy]-6-fluoro-, (1R,2R,3R,5R,6R)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



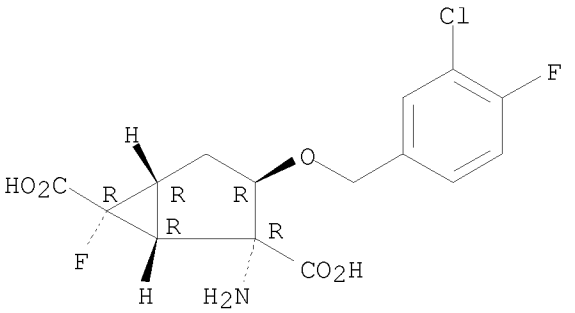
RN 569686-90-4 CAPLUS
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-3-[(4-chloro-3-fluorophenyl)methoxy]-6-fluoro-, (1R,2R,3R,5R,6R)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RN 569686-91-5 CAPLUS
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-3-[(3-chloro-4-fluorophenyl)methoxy]-6-fluoro-, (1R,2R,3R,5R,6R)- (CA INDEX NAME)

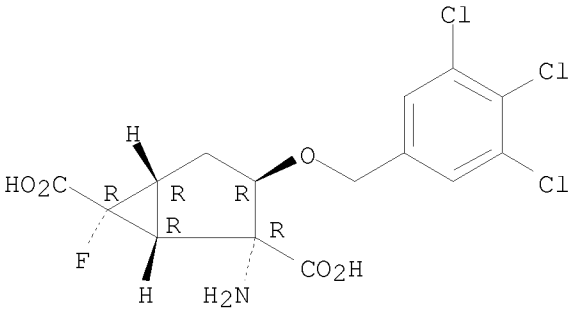
Absolute stereochemistry. Rotation (-).



RN 569686-92-6 CAPLUS

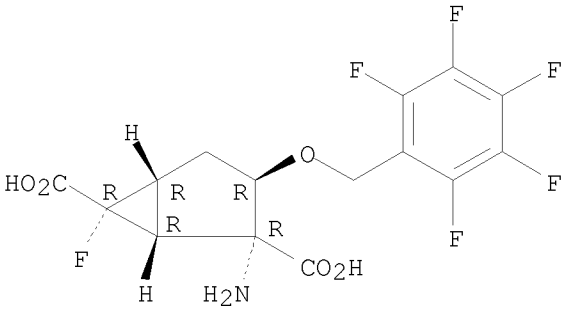
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid,
2-amino-6-fluoro-3-[(3,4,5-trichlorophenyl)methoxy]-, (1R,2R,3R,5R,6R)-
(CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

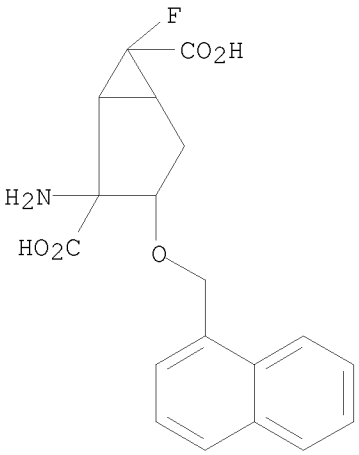


RN 569686-93-7 CAPLUS
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid,
2-amino-6-fluoro-3-[(2,3,4,5,6-pentafluorophenyl)methoxy]-,
(1R,2R,3R,5R,6R)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

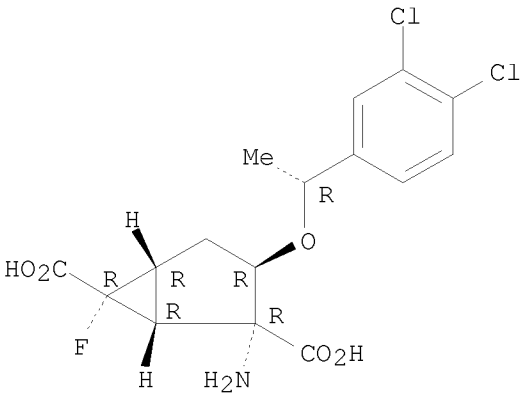


RN 569686-94-8 CAPLUS
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid,
2-amino-6-fluoro-3-(1-naphthalenylmethoxy)-, (1R,2R,3R,5R,6R)- (CA INDEX
NAME)



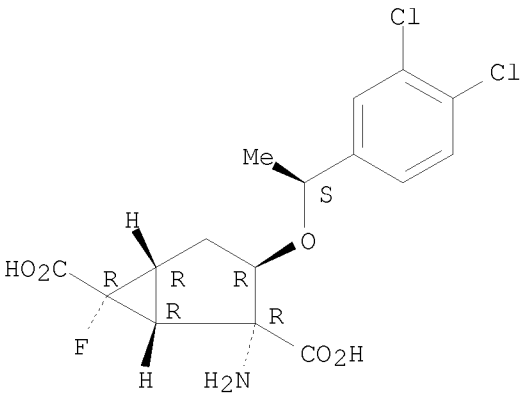
RN 569686-99-3 CAPLUS
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid,
2-amino-3-[(1R)-1-(3,4-dichlorophenyl)ethoxy]-6-fluoro-, (1R,2R,3R,5R,6R)-
(CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



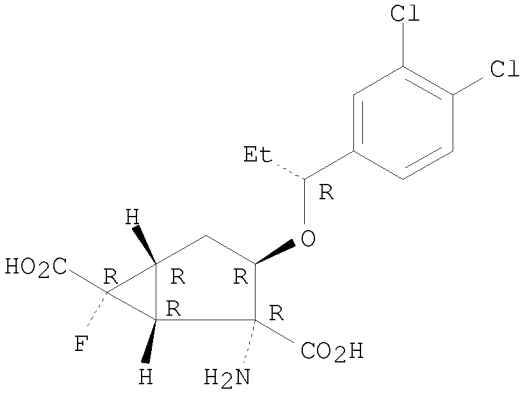
RN 569687-00-9 CAPLUS
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid,
2-amino-3-[(1S)-1-(3,4-dichlorophenyl)ethoxy]-6-fluoro-, (1R,2R,3R,5R,6R)-
(CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



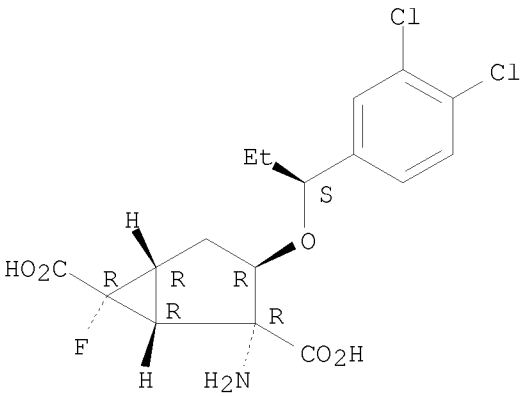
RN 569687-01-0 CAPLUS
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid,
2-amino-3-[(1R)-1-(3,4-dichlorophenyl)propoxy]-6-fluoro-,
(1R,2R,3R,5R,6R)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



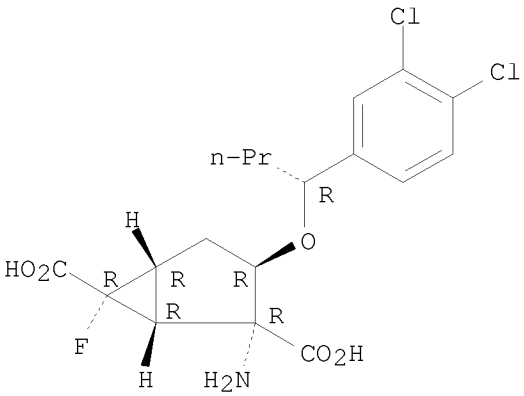
RN 569687-02-1 CAPLUS
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid,
2-amino-3-[(1S)-1-(3,4-dichlorophenyl)propoxy]-6-fluoro-,
(1R,2R,3R,5R,6R)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



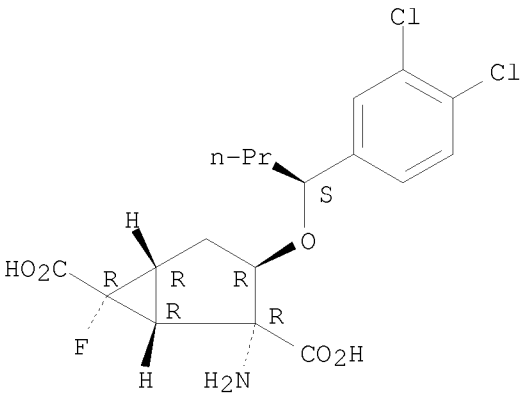
RN 569687-03-2 CAPLUS
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid,
2-amino-3-[(1R)-1-(3,4-dichlorophenyl)butoxy]-6-fluoro-, (1R,2R,3R,5R,6R)-
(CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



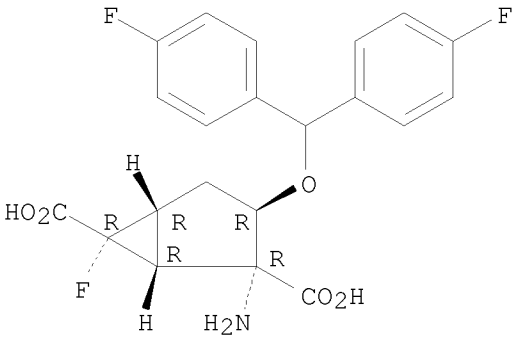
RN 569687-04-3 CAPLUS
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid,
2-amino-3-[(1S)-1-(3,4-dichlorophenyl)butoxy]-6-fluoro-, (1R,2R,3R,5R,6R)-
(CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



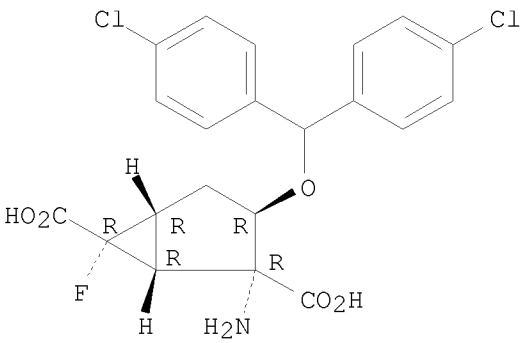
RN 569687-06-5 CAPLUS
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-3-[bis(4-fluorophenyl)methoxy]-6-fluoro-, (1R,2R,3R,5R,6R)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



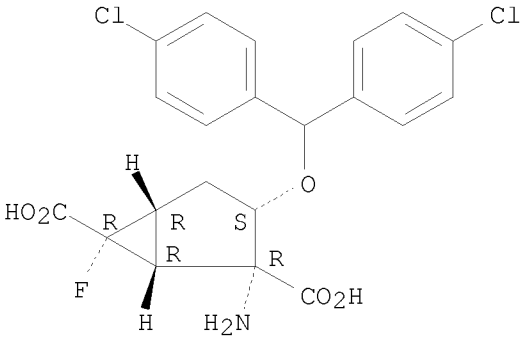
RN 569687-07-6 CAPLUS
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-3-[bis(4-chlorophenyl)methoxy]-6-fluoro-, (1R,2R,3R,5R,6R)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



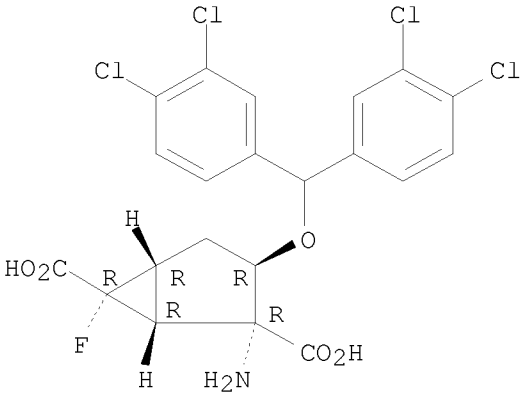
RN 569687-08-7 CAPLUS
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-3-[bis(4-chlorophenyl)methoxy]-6-fluoro-, (1R,2R,3S,5R,6R)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



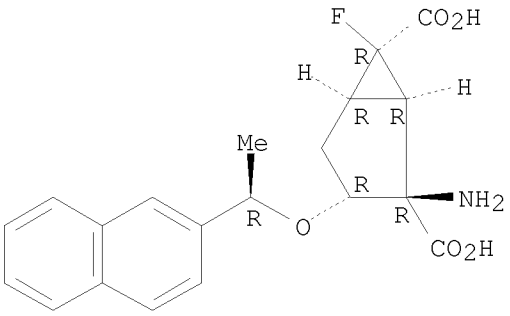
RN 569687-09-8 CAPLUS
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-3-[bis(3,4-dichlorophenyl)methoxy]-6-fluoro-, (1R,2R,3R,5R,6R)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



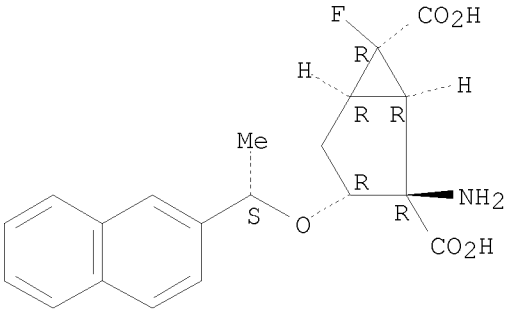
RN 569687-10-1 CAPLUS
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-6-fluoro-3-[(1R)-1-(2-naphthalenyl)ethoxy]-, (1R,2R,3R,5R,6R)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



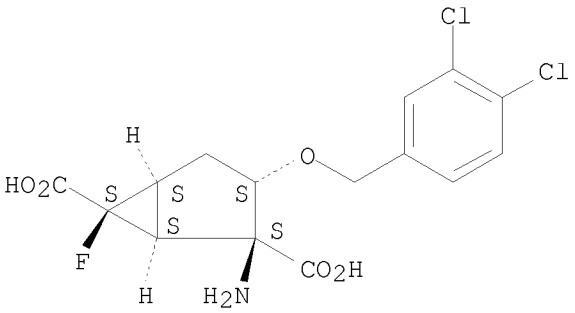
RN 569687-11-2 CAPLUS
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-6-fluoro-3-[(1S)-1-(2-naphthalenyl)ethoxy]-, (1R,2R,3R,5R,6R)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RN 748780-99-6 CAPLUS
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-3-[(3,4-dichlorophenyl)methoxy]-6-fluoro-, (1S,2S,3S,5S,6S)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

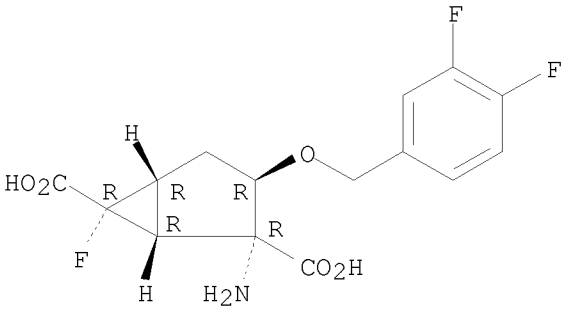


IT 569686-77-7P 569686-87-9P 569686-95-9P
569687-05-4P
RL: PAC (Pharmacological activity); PRP (Properties); SPN (Synthetic

preparation); BIOL (Biological study); PREP (Preparation)
(preparation of alkoxy(amino)fluorobicyclohexanedicarboxylic acid derivs. and their binding affinity of group II metabotropic glutamate receptors, pharamocokinetics, and SAR starting from chiral fluoro(oxo)bicyclohexanecarboxylates)

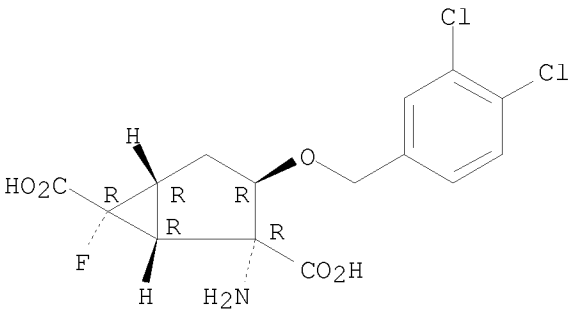
RN 569686-77-7 CAPLUS
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-3-[(3,4-difluorophenyl)methoxy]-6-fluoro-, (1R,2R,3R,5R,6R)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



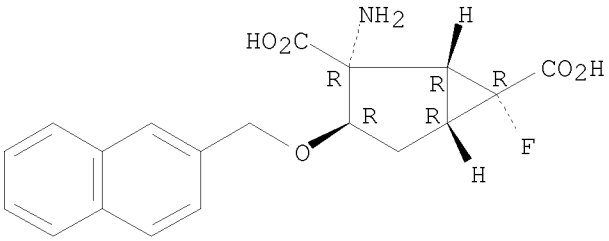
RN 569686-87-9 CAPLUS
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-3-[(3,4-dichlorophenyl)methoxy]-6-fluoro-, (1R,2R,3R,5R,6R)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



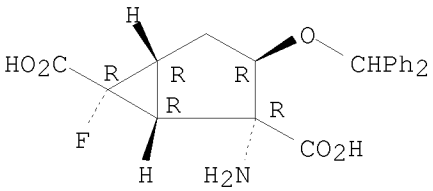
RN 569686-95-9 CAPLUS
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-6-fluoro-3-(2-naphthalenylmethoxy)-, (1R,2R,3R,5R,6R)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



RN 569687-05-4 CAPLUS
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-3-(diphenylmethoxy)-6-fluoro-, (1R,2R,3R,5R,6R)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



OS.CITING REF COUNT: 18 THERE ARE 18 CAPLUS RECORDS THAT CITE THIS RECORD (18 CITINGS)
REFERENCE COUNT: 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 21 OF 23 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2004:126085 CAPLUS
DOCUMENT NUMBER: 141:82129
TITLE: MGS0039: a potent and selective group II metabotropic glutamate receptor antagonist with antidepressant-like activity
AUTHOR(S): Chaki, Shigeyuki; Yoshikawa, Ryoko; Hirota, Shiho; Shimazaki, Toshiharu; Maeda, Maoko; Kawashima, Naoya; Yoshimizu, Takao; Yasuhara, Akito; Sakagami, Kazunari; Okuyama, Shigeru; Nakanishi, Shigetada; Nakazato, Atsuro
CORPORATE SOURCE: Medicinal Research Laboratories, Taisho Pharmaceutical Co., Ltd., Saitama, 331-9530, Japan
SOURCE: Neuropharmacology (2004), 46(4), 457-467
CODEN: NEPHBW; ISSN: 0028-3908
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The present study describes the pharmacol. profile of (1R,2R,3R,5R,6R)-2-Amino-3-(3,4-dichlorobenzyloxy)-6-fluorobicyclo[3.1.0]hexane-2,6-dicarboxylic acid (MGS0039), a novel group II mGluR antagonist. MGS0039 showed high affinity for both mGluR2 (Ki = 2.2 nM) and mGluR3 (Ki = 4.5 nM), which are comparable to LY341495, another group II mGluR antagonist. MGS0039 attenuated both glutamate-induced inhibition of forskolin-evoked cAMP formation in CHO

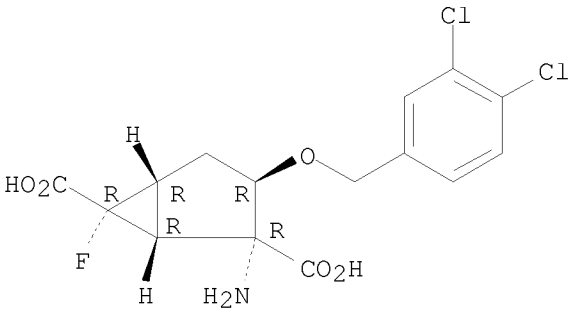
cells expressing mGluR2 (IC50 = 20 nM) or mGluR3 (IC50=24 nM) and glutamate-increased [35S]GTPγS binding to mGluR2 (pA2=8.2), which means that MGS0039 acts as an antagonist. MGS0039 shifted the dose-response curve of glutamate-increased [35S]GTPγS binding rightward without altering the maximal response, and thereby indicating competitive antagonism. MGS0039 showed no significant effects on other mGluRs as well as the other receptors and transporters we studied. MGS0039 (0.3-3 mg/kg, i.p.) as well as LY341495 (0.1-3 mg/kg, i.p.) had dose-dependent antidepressant-like effects in the rat forced swim test and in the mouse tail suspension test. In contrast, MGS0039 (0.3-3 mg/kg, i.p.) had no apparent effect in the rat social interaction test and in the rat elevated plus-maze. These results indicate that MGS0039 is a potent and selective antagonist of group II mGluR, and that group II mGluR antagonists, like MGS0039, have an antidepressant-like potential in exptl. animal models.

IT 569686-87-9, MGS 0039
RL: DMA (Drug mechanism of action); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(MGS0039: a potent and selective group II metabotropic glutamate receptor antagonist with antidepressant-like activity)

RN 569686-87-9 CAPLUS

CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-3-[(3,4-dichlorophenyl)methoxy]-6-fluoro-, (1R,2R,3R,5R,6R)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



OS.CITING REF COUNT: 55 THERE ARE 55 CAPLUS RECORDS THAT CITE THIS RECORD (55 CITINGS)

REFERENCE COUNT: 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 22 OF 23 CAPLUS COPYRIGHT 2009 ACS on STN

ACCESSION NUMBER: 2004:96754 CAPLUS

DOCUMENT NUMBER: 140:368470

TITLE: Increased cell proliferation in the adult mouse hippocampus following chronic administration of group II metabotropic glutamate receptor antagonist, MGS0039

AUTHOR(S): Yoshimizu, Takao; Chaki, Shigeyuki

CORPORATE SOURCE: Medicinal Research Laboratories, Medicinal Pharmacology Laboratory, Psychiatric Diseases and Pain Research, Taisho Pharmaceutical Co., Ltd., Kita-ku, Saitama, 331-9530, Japan

SOURCE: Biochemical and Biophysical Research Communications (2004), 315(2), 493-496
CODEN: BBRCA9; ISSN: 0006-291X
PUBLISHER: Elsevier Science
DOCUMENT TYPE: Journal
LANGUAGE: English

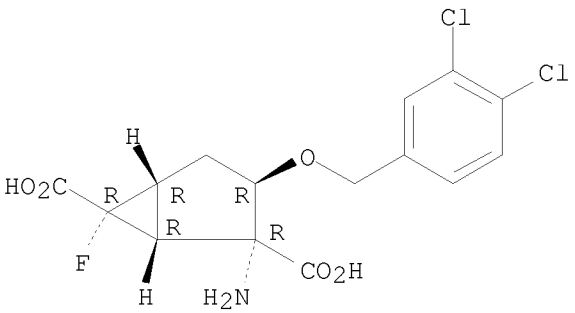
AB We have previously reported that MGS0039, a novel antagonist of group II metabotropic glutamate receptors (mGluRs), exerts antidepressant-like effects in exptl. animal models. Recent studies suggest that the behavioral effects of chronic antidepressant treatment are mediated by the stimulation of neurogenesis in the hippocampus. In the present study, we examined the effects of MGS0039 on cell proliferation in the adult mouse hippocampus. MGS0039 (5 or 10 mg/kg) or fluvoxamine was administered chronically to male ICR mice over a period of 14 days. Multiple bromodeoxyuridine (BrdU) administrations were performed after the last drug injection to label dividing cells. Immunohistochem. analyses after BrdU injections revealed that chronic MGS0039 treatment enhanced BrdU-pos. cells in the dentate gyrus (.apprx.62% increase) in the same manner as chronic fluvoxamine treatment. This is the first in vivo study to demonstrate an increase in cell proliferation following a blockade of group II mGluRs. These findings raise the possibility that MGS0039 may exert antidepressant-like effects by modulating cell proliferation in the hippocampus.

IT 569686-87-9, MGS 0039
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(chronic administration; increased cell proliferation in the adult mouse hippocampus following chronic administration of group II metabotropic glutamate receptor antagonist, MGS0039)

RN 569686-87-9 CAPLUS

CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-3-[(3,4-dichlorophenyl)methoxy]-6-fluoro-, (1R,2R,3R,5R,6R)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



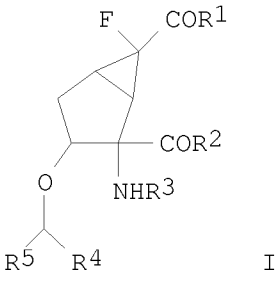
OS.CITING REF COUNT: 45 THERE ARE 45 CAPLUS RECORDS THAT CITE THIS RECORD (46 CITINGS)
REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 23 OF 23 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2003:591035 CAPLUS

DOCUMENT NUMBER: 139:143973
TITLE: 6-Fluorobicyclo[3.1.0]hexane derivatives
INVENTOR(S): Nakazato, Atsuro; Chaki, Shigeyuki; Sakagami, Kazunari; Dean, Ryoko; Ohta, Hiroshi; Hirota, Shiho; Yasuhara, Akito
PATENT ASSIGNEE(S): Taisho Pharmaceutical Co.,ltd., Japan
SOURCE: PCT Int. Appl., 98 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2003061698	A1	20030731	WO 2002-JP13693		20021226
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW					
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
CA 2471642	A1	20030731	CA 2002-2471642		20021226
EP 1459765	A1	20040922	EP 2002-793421		20021226
EP 1459765	B1	20080820			
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK					
BR 2002015462	A	20041130	BR 2002-15462		20021226
CN 1610557	A	20050427	CN 2002-826388		20021226
CN 1281274	C	20061025			
ZA 2005002085	A	20050629	ZA 2005-2085		20021226
HU 2004002649	A2	20051028	HU 2004-2649		20021226
NZ 533699	A	20060526	NZ 2002-533699		20021226
AU 2002359923	B2	20071220	AU 2002-359923		20021226
RU 2315622	C2	20080127	RU 2004-122916		20021226
AT 405289	T	20080915	AT 2002-793421		20021226
ES 2311642	T3	20090216	ES 2002-793421		20021226
JP 4230919	B2	20090225	JP 2003-561641		20021226
NO 2004002530	A	20040922	NO 2004-2530		20040616
ZA 2004004795	A	20050617	ZA 2004-4795		20040617
IN 2004CN01417	A	20060210	IN 2004-CN1417		20040623
MX 2004006322	A	20041004	MX 2004-6322		20040625
KR 897970	B1	20090518	KR 2004-710069		20040625
US 20050119345	A1	20050602	US 2005-500101		20050204
US 7157594	B2	20070102			
HK 1073258	A1	20070323	HK 2005-106035		20050715
KR 2009031962	A	20090330	KR 2009-705135		20090312
PRIORITY APPLN. INFO.:			JP 2001-395797	A	20011227
			WO 2002-JP13693	W	20021226
			KR 2004-710069	A3	20040625

OTHER SOURCE(S): MARPAT 139:143973
GI



I

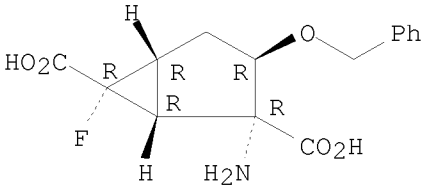
AB Antidepressants containing as the active ingredient compds. having group II metabotropic glutamate receptor antagonism; and 2-amino-3-alkoxy-6-fluorobicyclo[3.1.0]- hexane-2,6-dicarboxylic acid derivs. represented by the general formula [I], pharmaceutically acceptable salts thereof, or hydrates of the salts: I wherein R1 and R2 may be the same or different from each other and are each hydroxyl, C1-10 alkoxy, or the like; R3 is C1-10 acyl, C1-6 alkoxy-C1-6 acyl, or the like; and R4 and R5 may be the same or different from each other and are each hydrogen, C1-10 alkyl, or the like.

IT 569686-59-5P 569686-61-9P 569686-62-0P
569686-63-1P 569686-64-2P 569686-65-3P
569686-66-4P 569686-67-5P 569686-68-6P
569686-69-7P 569686-70-0P 569686-71-1P
569686-72-2P 569686-73-3P 569686-74-4P
569686-75-5P 569686-76-6P 569686-77-7P
569686-78-8P 569686-79-9P 569686-80-2P
569686-81-3P 569686-82-4P 569686-83-5P
569686-84-6P 569686-85-7P 569686-86-8P
569686-87-9P 569686-88-0P 569686-89-1P
569686-90-4P 569686-91-5P 569686-92-6P
569686-93-7P 569686-94-8P 569686-95-9P
569686-98-2P 569686-99-3P 569687-00-9P
569687-01-0P 569687-02-1P 569687-03-2P
569687-04-3P 569687-05-4P 569687-06-5P
569687-07-6P 569687-08-7P 569687-09-8P
569687-10-1P 569687-11-2P 569687-13-4P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(6-Fluorobicyclo[3.1.0]hexane derivs. having group II metabotropic glutamate receptor antagonist actions as antidepressants)

RN 569686-59-5 CAPLUS

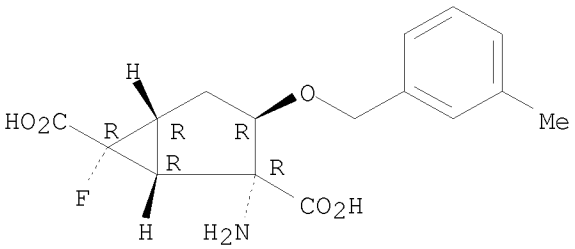
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-6-fluoro-3-(phenylmethoxy)-, (1R,2R,3R,5R,6R)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



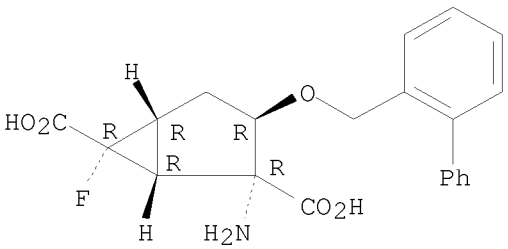
RN 569686-61-9 CAPLUS
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-6-fluoro-3-[(3-methylphenyl)methoxy]-, (1R,2R,3R,5R,6R)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



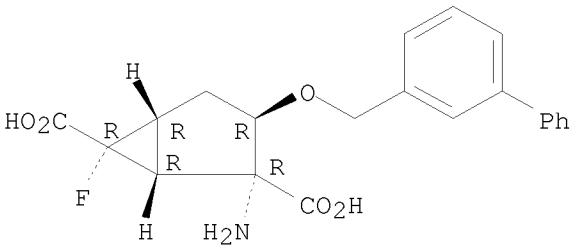
RN 569686-62-0 CAPLUS
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-3-([1,1'-biphenyl]-2-ylmethoxy)-6-fluoro-, (1R,2R,3R,5R,6R)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



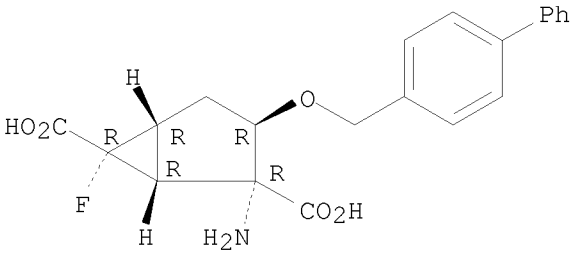
RN 569686-63-1 CAPLUS
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-3-([1,1'-biphenyl]-3-ylmethoxy)-6-fluoro-, (1R,2R,3R,5R,6R)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



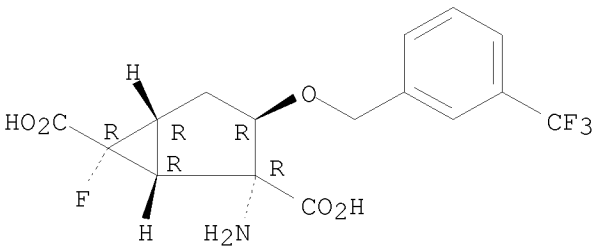
RN 569686-64-2 CAPLUS
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-3-([1,1'-biphenyl]-4-ylmethoxy)-6-fluoro-, (1R,2R,3R,5R,6R)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



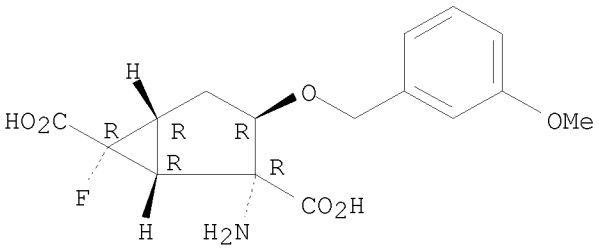
RN 569686-65-3 CAPLUS
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-6-fluoro-3-[[3-(trifluoromethyl)phenyl]methoxy]-, (1R,2R,3R,5R,6R)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



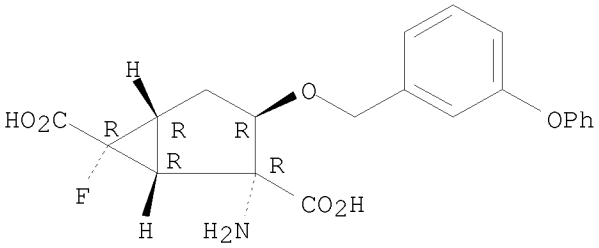
RN 569686-66-4 CAPLUS
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-6-fluoro-3-[(3-methoxyphenyl)methoxy]-, (1R,2R,3R,5R,6R)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



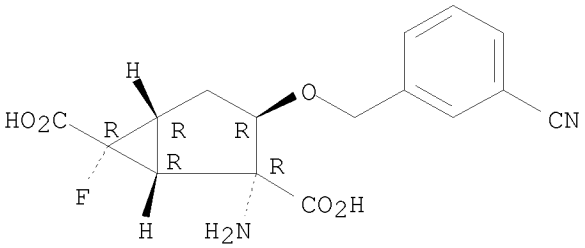
RN 569686-67-5 CAPLUS
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-6-fluoro-3-[(3-phenoxyphenyl)methoxy]-, (1R,2R,3R,5R,6R)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



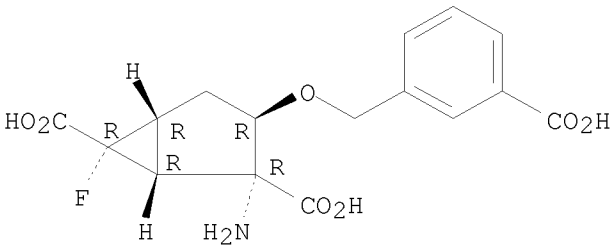
RN 569686-68-6 CAPLUS
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-3-[(3-cyanophenyl)methoxy]-6-fluoro-, (1R,2R,3R,5R,6R)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



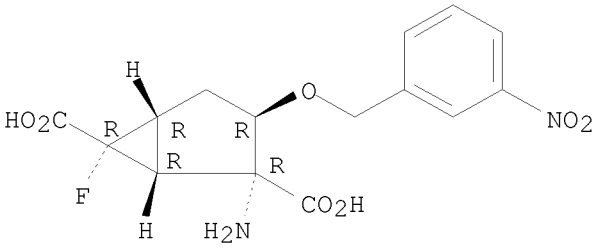
RN 569686-69-7 CAPLUS
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-3-[(3-carboxyphenyl)methoxy]-6-fluoro-, (1R,2R,3R,5R,6R)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



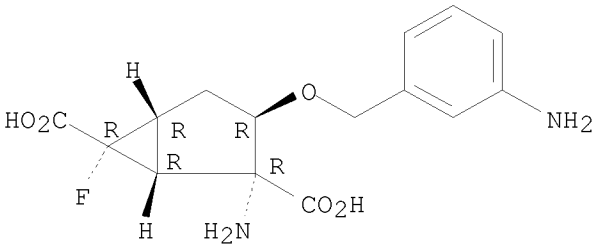
RN 569686-70-0 CAPLUS
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-6-fluoro-3-[(3-nitrophenyl)methoxy]-, (1R,2R,3R,5R,6R)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



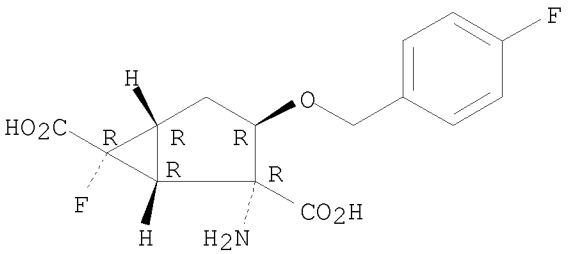
RN 569686-71-1 CAPLUS
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-3-[(3-aminophenyl)methoxy]-6-fluoro-, (1R,2R,3R,5R,6R)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



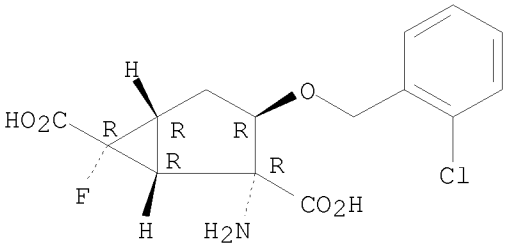
RN 569686-72-2 CAPLUS
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-6-fluoro-3-[(4-fluorophenyl)methoxy]-, (1R,2R,3R,5R,6R)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



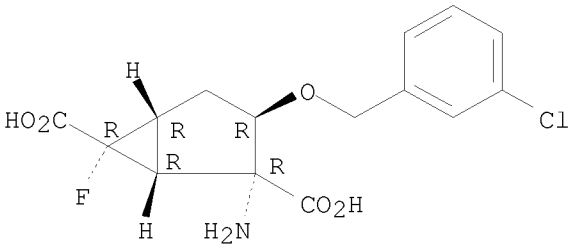
RN 569686-73-3 CAPLUS
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-3-[(2-chlorophenyl)methoxy]-6-fluoro-, (1R,2R,3R,5R,6R)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



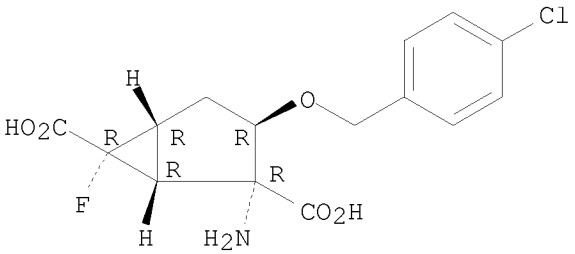
RN 569686-74-4 CAPLUS
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-3-[(3-chlorophenyl)methoxy]-6-fluoro-, (1R,2R,3R,5R,6R)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



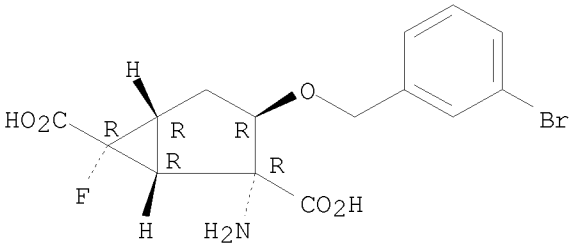
RN 569686-75-5 CAPLUS
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-3-[(4-chlorophenyl)methoxy]-6-fluoro-, (1R,2R,3R,5R,6R)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



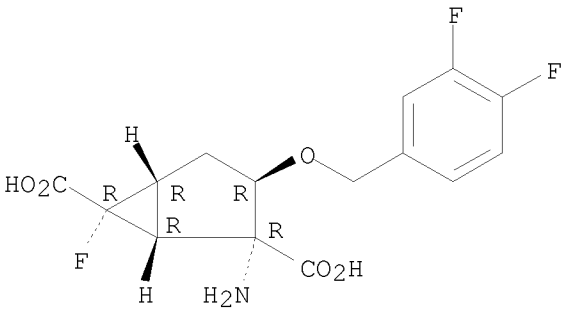
RN 569686-76-6 CAPLUS
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-3-[(3-bromophenyl)methoxy]-6-fluoro-, (1R,2R,3R,5R,6R)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



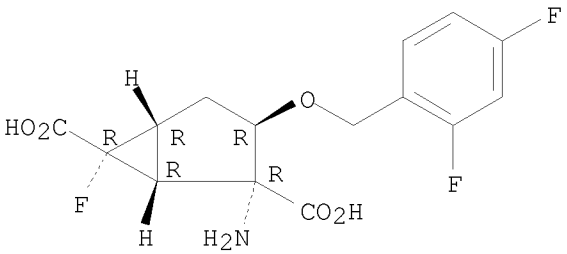
RN 569686-77-7 CAPLUS
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-3-[(3,4-difluorophenyl)methoxy]-6-fluoro-, (1R,2R,3R,5R,6R)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



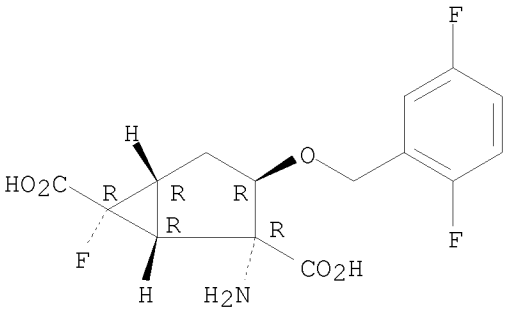
RN 569686-78-8 CAPLUS
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-3-[(2,4-difluorophenyl)methoxy]-6-fluoro-, (1R,2R,3R,5R,6R)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



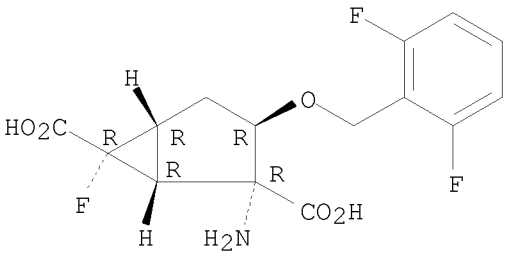
RN 569686-79-9 CAPLUS
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-3-[(2,5-difluorophenyl)methoxy]-6-fluoro-, (1R,2R,3R,5R,6R)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



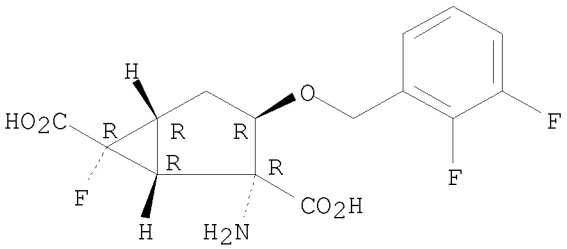
RN 569686-80-2 CAPLUS
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-3-[(2,6-difluorophenyl)methoxy]-6-fluoro-, (1R,2R,3R,5R,6R)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



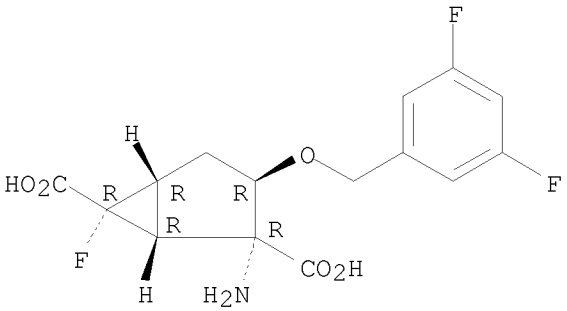
RN 569686-81-3 CAPLUS
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-3-[(2,3-difluorophenyl)methoxy]-6-fluoro-, (1R,2R,3R,5R,6R)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



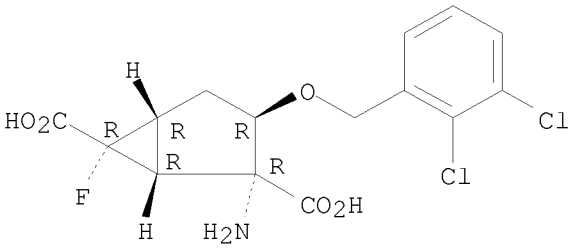
RN 569686-82-4 CAPLUS
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-3-[(3,5-difluorophenyl)methoxy]-6-fluoro-, (1R,2R,3R,5R,6R)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



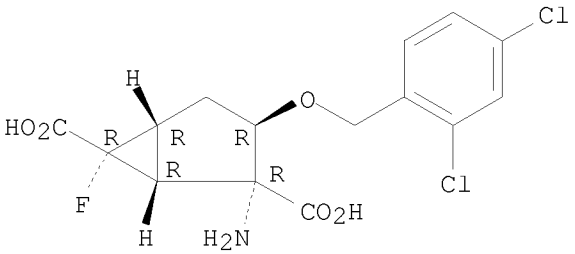
RN 569686-83-5 CAPLUS
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-3-[(2,3-dichlorophenyl)methoxy]-6-fluoro-, (1R,2R,3R,5R,6R)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



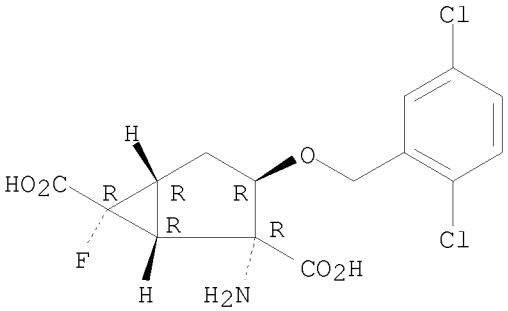
RN 569686-84-6 CAPLUS
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-3-[(2,4-dichlorophenyl)methoxy]-6-fluoro-, (1R,2R,3R,5R,6R)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



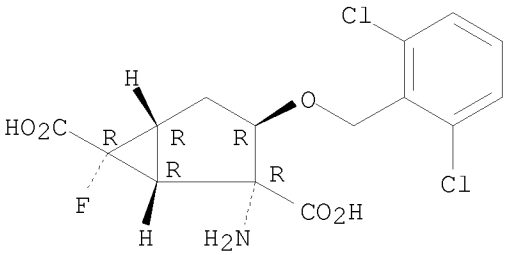
RN 569686-85-7 CAPLUS
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-3-[(2,5-dichlorophenyl)methoxy]-6-fluoro-, (1R,2R,3R,5R,6R)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



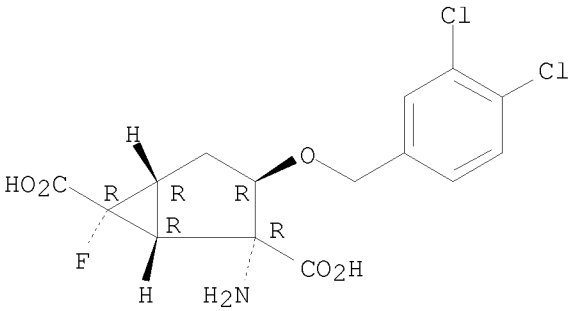
RN 569686-86-8 CAPLUS
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-3-[(2,6-dichlorophenyl)methoxy]-6-fluoro-, (1R,2R,3R,5R,6R)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



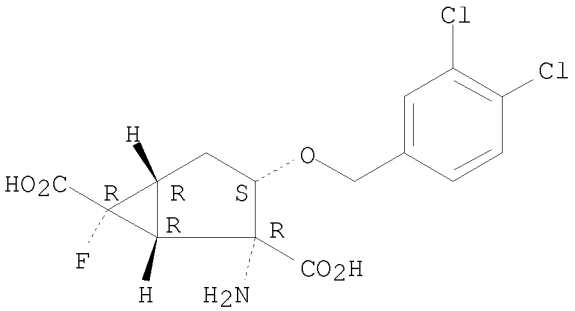
RN 569686-87-9 CAPLUS
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-3-[(3,4-dichlorophenyl)methoxy]-6-fluoro-, (1R,2R,3R,5R,6R)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



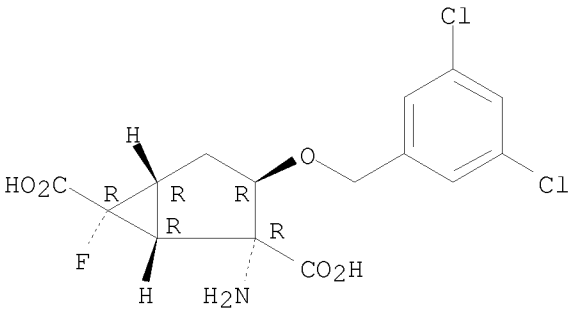
RN 569686-88-0 CAPLUS
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-3-[(3,4-dichlorophenyl)methoxy]-6-fluoro-, (1R,2R,3S,5R,6R)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RN 569686-89-1 CAPLUS
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-3-[(3,5-dichlorophenyl)methoxy]-6-fluoro-, (1R,2R,3R,5R,6R)- (CA INDEX NAME)

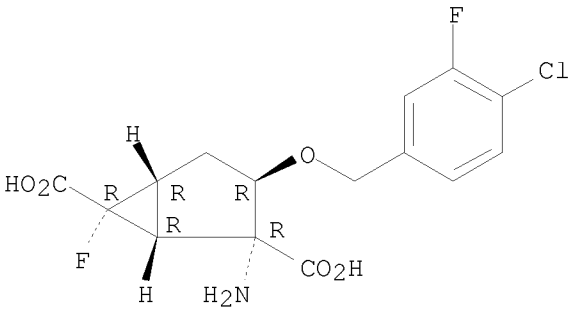
Absolute stereochemistry. Rotation (-).



RN 569686-90-4 CAPLUS
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-3-[(4-chloro-3-fluorophenyl)methoxy]-6-fluoro-, (1R,2R,3R,5R,6R)-

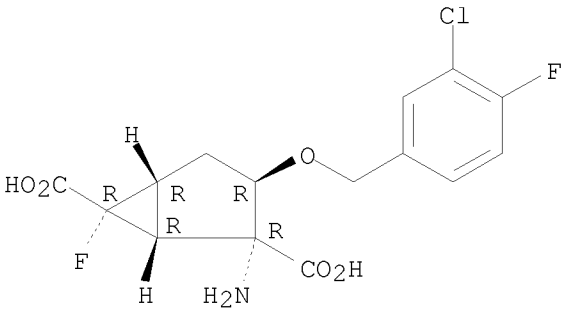
(CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



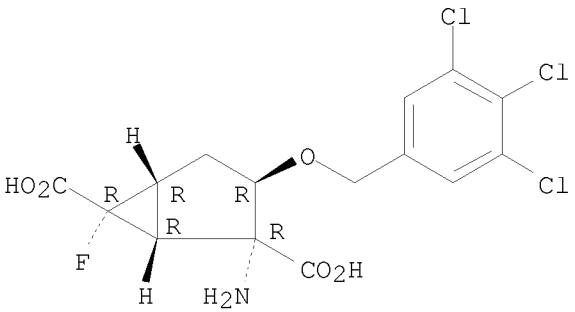
RN 569686-91-5 CAPLUS
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid,
2-amino-3-[(3-chloro-4-fluorophenyl)methoxy]-6-fluoro-, (1R,2R,3R,5R,6R)-
(CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



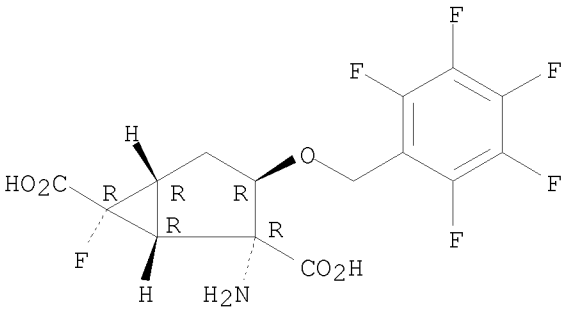
RN 569686-92-6 CAPLUS
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid,
2-amino-6-fluoro-3-[(3,4,5-trichlorophenyl)methoxy]-, (1R,2R,3R,5R,6R)-
(CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

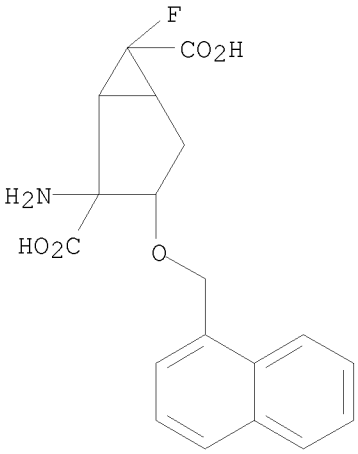


RN 569686-93-7 CAPLUS
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-6-fluoro-3-[(2,3,4,5,6-pentafluorophenyl)methoxy]-, (1R,2R,3R,5R,6R)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).

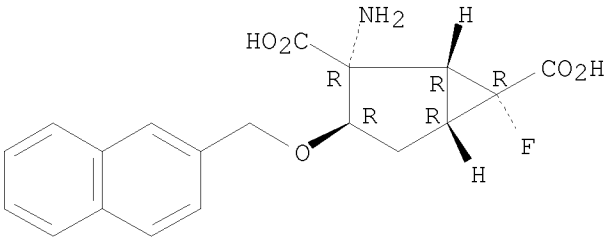


RN 569686-94-8 CAPLUS
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-6-fluoro-3-(1-naphthalenylmethoxy)-, (1R,2R,3R,5R,6R)- (CA INDEX NAME)



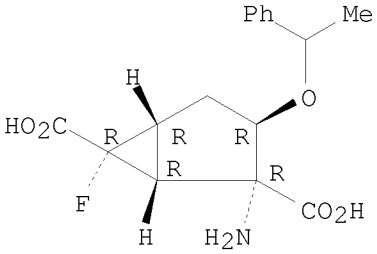
RN 569686-95-9 CAPLUS
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-6-fluoro-3-(2-naphthalenylmethoxy)-, (1R,2R,3R,5R,6R)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



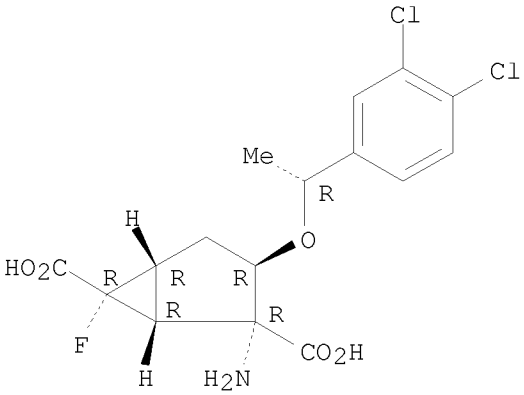
RN 569686-98-2 CAPLUS
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid,
2-amino-6-fluoro-3-(1-phenylethoxy)-, (1R,2R,3R,5R,6R)- (CA INDEX NAME)

Absolute stereochemistry.



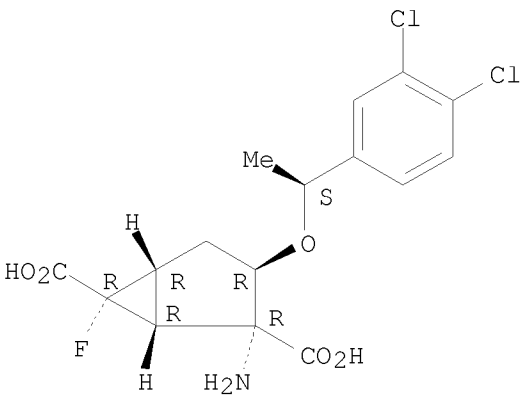
RN 569686-99-3 CAPLUS
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid,
2-amino-3-[(1R)-1-(3,4-dichlorophenyl)ethoxy]-6-fluoro-, (1R,2R,3R,5R,6R)-
(CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



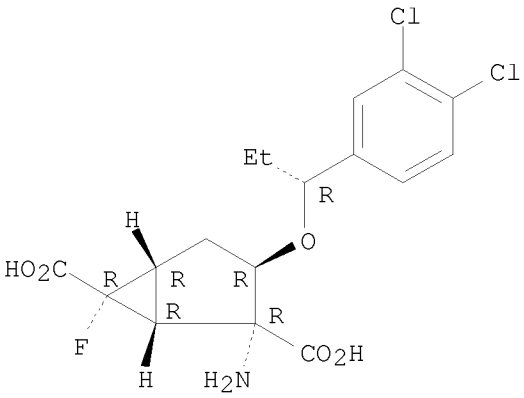
RN 569687-00-9 CAPLUS
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid,
2-amino-3-[(1S)-1-(3,4-dichlorophenyl)ethoxy]-6-fluoro-, (1R,2R,3R,5R,6R)-
(CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



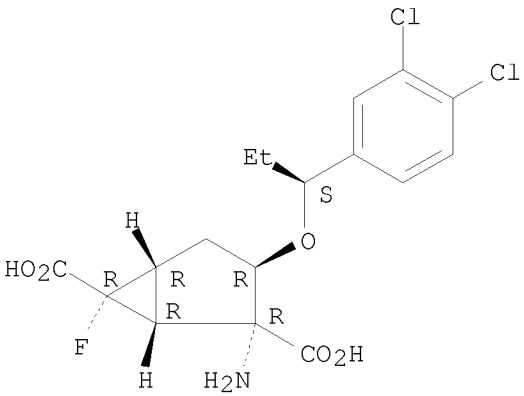
RN 569687-01-0 CAPLUS
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid,
2-amino-3-[(1R)-1-(3,4-dichlorophenyl)propoxy]-6-fluoro-,
(1R,2R,3R,5R,6R)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



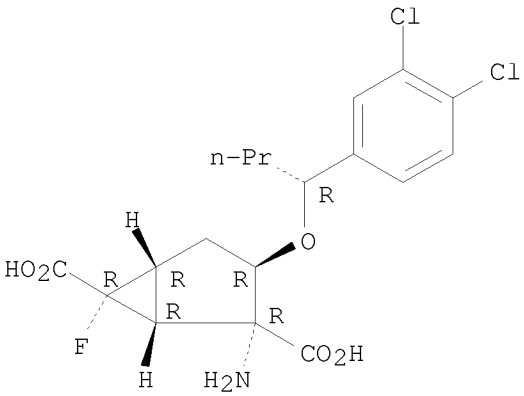
RN 569687-02-1 CAPLUS
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid,
2-amino-3-[(1S)-1-(3,4-dichlorophenyl)propoxy]-6-fluoro-,
(1R,2R,3R,5R,6R)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



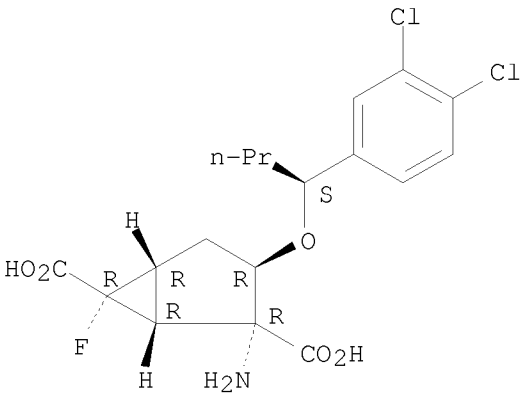
RN 569687-03-2 CAPLUS
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid,
2-amino-3-[(1R)-1-(3,4-dichlorophenyl)butoxy]-6-fluoro-, (1R,2R,3R,5R,6R)-
(CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



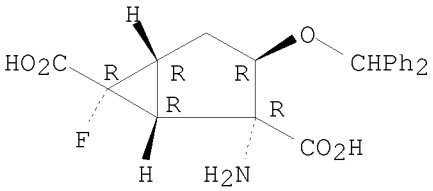
RN 569687-04-3 CAPLUS
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid,
2-amino-3-[(1S)-1-(3,4-dichlorophenyl)butoxy]-6-fluoro-, (1R,2R,3R,5R,6R)-
(CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



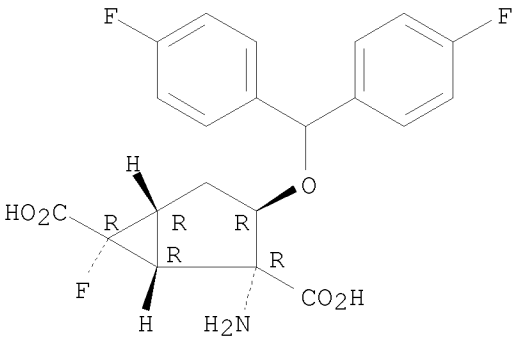
RN 569687-05-4 CAPLUS
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-3-(diphenylmethoxy)-6-fluoro-, (1R,2R,3R,5R,6R)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



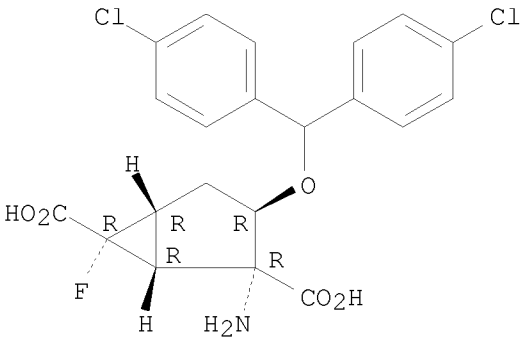
RN 569687-06-5 CAPLUS
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-3-[bis(4-fluorophenyl)methoxy]-6-fluoro-, (1R,2R,3R,5R,6R)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



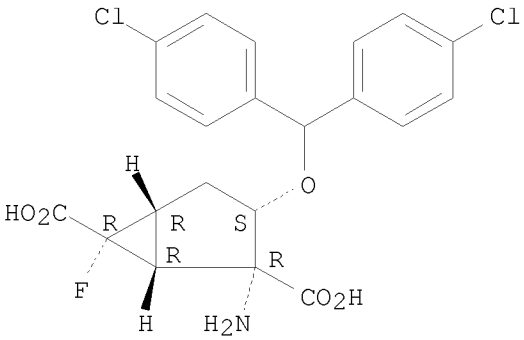
RN 569687-07-6 CAPLUS
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-3-[bis(4-chlorophenyl)methoxy]-6-fluoro-, (1R,2R,3R,5R,6R)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



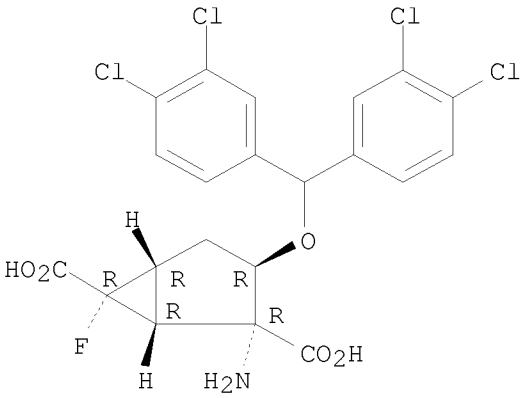
RN 569687-08-7 CAPLUS
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-3-[bis(4-chlorophenyl)methoxy]-6-fluoro-, (1R,2R,3S,5R,6R)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



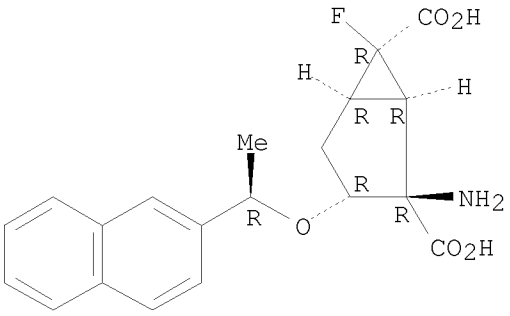
RN 569687-09-8 CAPLUS
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-3-[bis(3,4-dichlorophenyl)methoxy]-6-fluoro-, (1R,2R,3R,5R,6R)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



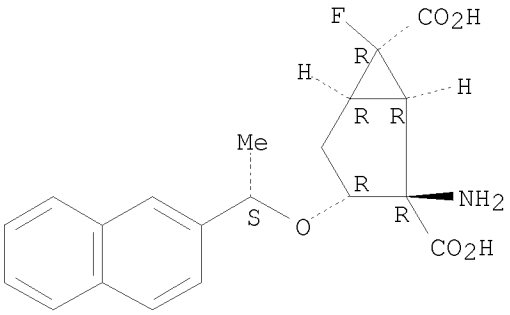
RN 569687-10-1 CAPLUS
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-6-fluoro-3-[(1R)-1-(2-naphthalenyl)ethoxy]-, (1R,2R,3R,5R,6R)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



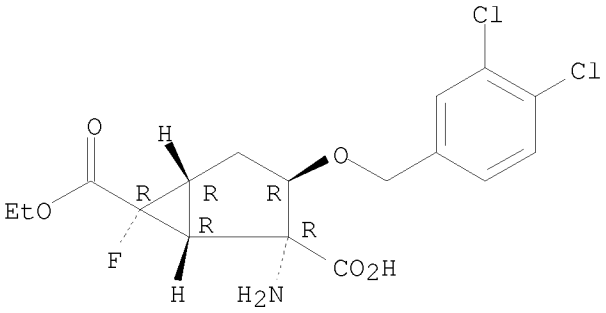
RN 569687-11-2 CAPLUS
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-6-fluoro-3-[(1S)-1-(2-naphthalenyl)ethoxy]-, (1R,2R,3R,5R,6R)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RN 569687-13-4 CAPLUS
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid,
2-amino-3-[(3,4-dichlorophenyl)methoxy]-6-fluoro-, 6-ethyl ester,
(1R,2R,3R,5R,6R)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



OS.CITING REF COUNT: 2 THERE ARE 2 CAPLUS RECORDS THAT CITE THIS RECORD (2 CITINGS)
REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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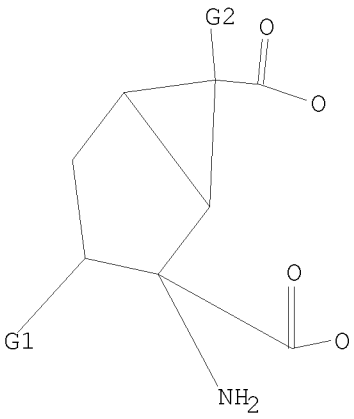

G1 O,S,N
G2 X,H

Structure attributes must be viewed using STN Express query preparation.

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Substance data SEARCH and crossover from CAS REGISTRY in progress...
Use DISPLAY HITSTR (or FHITSTR) to directly view retrieved structures.



SAMPLE SEARCH INITIATED 16:24:49 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED -       21 TO ITERATE

100.0% PROCESSED       21 ITERATIONS                              15 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:          146 TO      694
PROJECTED ANSWERS:              68 TO      532

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L13         11 L12

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L14          2 L13 AND PY<2003

=> d 1-2 ibib abs hitstr
THE ESTIMATED COST FOR THIS REQUEST IS 11.28 U.S. DOLLARS
DO YOU WANT TO CONTINUE WITH THIS REQUEST? (Y)/N:y

L14  ANSWER 1 OF 2  CAPLUS  COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER:        2000:157966  CAPLUS
DOCUMENT NUMBER:         132:166520
TITLE:                   Stereospecific synthesis of
                         2-amino-bicyclo[3.1.0]hexan-2,6-dicarboxylic acid
                         derivatives for use as metabotropic glutamate receptor
                         ligands
INVENTOR(S):             Adam, Geo; Huguenin-Virchaux, Philippe Nicolas; Mutel,
                         Vincent; Stadler, Heinz; Woltering, Thomas Johannes
PATENT ASSIGNEE(S):      F. Hoffmann-La Roche A.-G., Switz.
SOURCE:                  Ger. Offen., 22 pp.
                         CODEN: GWXXBX
DOCUMENT TYPE:           Patent
LANGUAGE:                German
FAMILY ACC. NUM. COUNT:  1
PATENT INFORMATION:

     PATENT NO.          KIND   DATE        APPLICATION NO.        DATE
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     DE 19941675          A1    20000309    DE 1999-19941675       19990901 <--
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CH 694053	A5	20040630	CH 1999-1550		19990824	
US 6107342	A	20000822	US 1999-385935		19990830	<--
CA 2281272	A1	20000303	CA 1999-2281272		19990831	<--
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SE 9903088	A	20000304	SE 1999-3088		19990901	<--
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IT 99MI1860	A1	20010301	IT 1999-MI1860		19990901	<--
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NL 1012963	C2	20031023				
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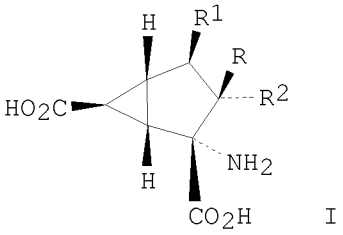
AU 757939	B2	20030313				
AT 501853	A1	20061115	AT 1999-1514		19990902	
BE 1014616	A3	20040203	BE 1999-595		19990903	

PRIORITY APPLN. INFO.: EP 1998-116670 A 19980903
OTHER SOURCE(S): MARPAT 132:166520
GI



I

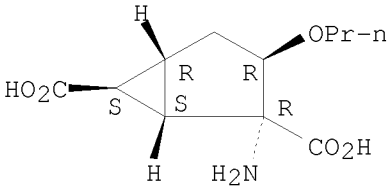
AB Title compds. [(I); R = OH, alkoxy, alkenyloxy, PhCH2O-, H, 2H, 3H; R1 = H, 3H; R,R1 = bond; R2 = H, 2H, 3H, OH, NH2] were stereospecifically prepared for use in treatment of neurol. conditions and psychiatric disturbances (no data). Thus, racemic Et (1α,5α,6α)-2-oxo-bicyclo[3.1.0]hexane-6-carboxylic acid was reacted with Ph bis((trifluoromethyl)sulfonyl)amine and the resulting triflate transformed into the racemic 2-ethyl-6-benzyl bicyclo[3.1.0]hex-2-ene-2,6-dicarboxylic acid, reaction of which with K2[OsO2(OH)4] gave stereospecifically the 1S,2S,3R,6S-diol, which could be isolated in 26% yield, at >99% enantiomeric excess. Preparation of the 2R-2-azido compound from the diol through a cyclic sulfate gave an intermediate which could then be alkylated, aminated, hydrogenated, de-esterified, or otherwise treated to give I, for use as ligands for metabotropic glutamate group II receptors.

IT 259134-96-8P
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(stereospecific synthesis of 2-amino-bicyclo[3.1.0]hexan-2,6-dicarboxylic acid derivs. for use as metabotropic glutamate receptor ligands)

RN 259134-96-8 CAPLUS

CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-3-propoxy-, (1S,2R,3R,5R,6S)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



OS.CITING REF COUNT: 10 THERE ARE 10 CAPLUS RECORDS THAT CITE THIS RECORD (27 CITINGS)

L14 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2000:68447 CAPLUS
DOCUMENT NUMBER: 132:93652
TITLE: Preparation of 2-aminobicyclo[3.1.0]hexane-2,6-dicarboxylates and related compounds as pharmaceutical intermediates and modulators of metabotropic glutamate receptor function.
INVENTOR(S): Baker, Stephen Richard; Monn, James Allen; Ezquerra Carrera, Jesus; Dominguez Fernandez, Carmen
PATENT ASSIGNEE(S): Eli Lilly and Company Limited, UK; Lilly, S.A.; Eli Lilly and Company
SOURCE: PCT Int. Appl., 48 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2000004010	A1	20000127	WO 1999-GB2273		19990714 <--
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RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG					
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EP 1097149	A1	20010509	EP 1999-933048		19990714 <--
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OTHER SOURCE(S): MARPAT 132:93652

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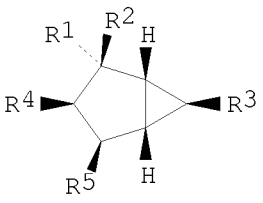


I

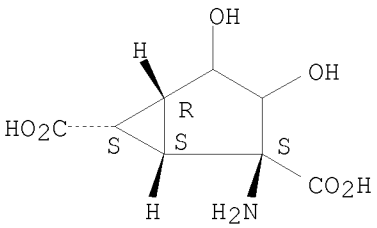
AB Title compds. [I; either R1 = N3, (protected) amino; R2 = (protected) carboxy; or R1 = trihalomethyl; R2 = OH; R3 = (protected) carboxy; either R4 = OR6 and R5 = OR7; or R4 and R5 = H or R4R5 = bond; ether R6 and R7 = H; or R6R7 = diol protecting group; provided that when R4 and R5 = H, R1 ≠ amino], were prepared s pharmaceutical intermediates and modulators of metabotropic glutamate receptor function (no data). Thus, ethoxycarbonylmethyldimethylsulfonium bromide in CHCl3 was treated with DBU and then with (-)-2,3-(cyclohexylidenedioxy)-4-cyclopentenone in CHCl3 followed by stirring overnight to give 96% Et (1S,3R,4R,5R,6S)-2-oxo-3,4-cyclohexylidenedioxybicyclo[3.1.0]hexane-6-carboxylate. This with CHCl3 in THF at -78° was treated with Li hexamethyldisilazide in THF followed by warming to room temperature to give 94% Et (1S,2S,3R,4R,5R,6S)-2-trichloromethyl-2-hydroxy-3,4-cyclohexylidenedioxybicyclo[3.1.0]hexane-6-carboxylate. Treatment of the latter with NaN3, 18-crown-6, and DBU in MeOH over 6 h gave 84% di-Me (1S,2R,3S,4R,5R,6S)-2-azido-3,4-cyclohexylidenedioxybicyclo[3.1.0]hexane-2,6-dicarboxylate. This was hydrogenated in EtOAc over Pd/C to give 71% of the corresponding amine, which was converted to (1S,2R,3S,4R,5R,6R)-2-amino-3,4-dihydroxybicyclo[3.1.0]hexane-2,6-dicarboxylic acid in several steps.

IT 254982-43-9P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 2-aminobicyclo[3.1.0]hexane-2,6-dicarboxylates and related compds. as pharmaceutical intermediates and modulators of metabotropic glutamate receptor function)

RN 254982-43-9 CAPLUS

CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-3,4-dihydroxy-, (1S,2S,5R,6S)- (CA INDEX NAME)

Absolute stereochemistry.



OS.CITING REF COUNT: 3 THERE ARE 3 CAPLUS RECORDS THAT CITE THIS RECORD (3 CITINGS)
REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> s l11 sss full
REG1stRY INITIATED
Substance data SEARCH and crossover from CAS REGISTRY in progress...
Use DISPLAY HITSTR (or FHITSTR) to directly view retrieved structures.

THE ESTIMATED SEARCH COST FOR FILE 'REGISTRY' IS 185.40 U.S. DOLLARS
DO YOU WANT TO CONTINUE WITH THIS REQUEST? (Y)/N or END:y
FULL SEARCH INITIATED 16:26:44 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 504 TO ITERATE

100.0% PROCESSED 504 ITERATIONS 332 ANSWERS
SEARCH TIME: 00.00.01

L15 332 SEA SSS FUL L11

L16 29 L15

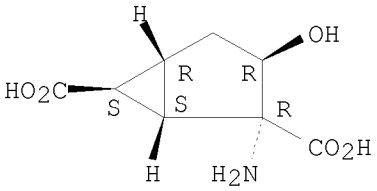
=> s l16 and py<2003
22984598 PY<2003
L17 4 L16 AND PY<2003

=> d 1-4 ibib abs hitstr
THE ESTIMATED COST FOR THIS REQUEST IS 22.56 U.S. DOLLARS
DO YOU WANT TO CONTINUE WITH THIS REQUEST? (Y)/N:y

L17 ANSWER 1 OF 4 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2002:851222 CAPLUS
DOCUMENT NUMBER: 138:198858
TITLE: Molecular docking of ligands of glutamate receptors
AUTHOR(S): Belenikin, M. S.; Makkiarulo, A.; Konstantino, G.; Palyulin, V. A.; Pellichari, P.; Zefirov, N. S.
CORPORATE SOURCE: Kafedra Org. Khim., Mosk. Gos. Univ., Moscow, Russia
SOURCE: Vestnik Moskovskogo Universiteta, Seriya 2: Khimiya (2002), 43(4), 221-230
CODEN: VMUKA5; ISSN: 0579-9384
PUBLISHER: Izdatel'stvo Moskovskogo Universiteta
DOCUMENT TYPE: Journal
LANGUAGE: Russian
AB Docking of a number of agonists and antagonists into glutamate-binding sites of human metabotropic and ionotropic glutamate receptors was modeled using the computer program AutoDock 3.0. The three-dimensional structures of the ligand-receptor complexes were in good agreement with exptl. data. Effect of water mols. at the ligand-binding site of the receptor on the ligand orientation was studied.

IT 259134-85-5
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(modeling of mol. docking of ligands of human metabotropic and ionotropic glutamate receptors)
RN 259134-85-5 CAPLUS
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-3-hydroxy-, (1S,2R,3R,5R,6S)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).

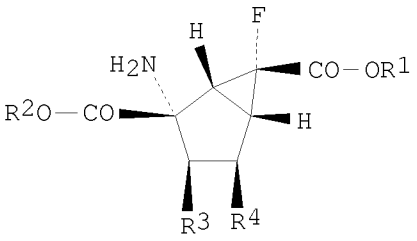


L17 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2002:10425 CAPLUS
DOCUMENT NUMBER: 136:85627
TITLE: Preparation of bicyclo[3.1.0]dicarboxylic acid derivatives as group 2 metabotropic glutamate receptor agonists
INVENTOR(S): Nakazato, Atsuro; Kumagai, Toshihito; Kanuma, Kosuke; Sakagami, Kazunari
PATENT ASSIGNEE(S): Taisho Pharmaceutical Co., Ltd., Japan
SOURCE: PCT Int. Appl., 25 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002000605	A1	20020103	WO 2001-JP5550	20010628 <--
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 2001067854	A	20020108	AU 2001-67854	20010628 <--
CA 2411059	A1	20021206	CA 2001-2411059	20010628 <--
EP 1295865	A1	20030326	EP 2001-945657	20010628
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
CN 1216038	C	20050824	CN 2001-811723	20010628
AU 2001267854	B2	20051201	AU 2001-267854	20010628

US 20030134902	A1	20030717	US 2002-297479		20021206
US 6770676	B2	20040803			
HK 1056868	A1	20051202	HK 2003-109245		20031219
PRIORITY APPLN. INFO.:			JP 2000-195239	A	20000628
			WO 2001-JP5550	W	20010628

OTHER SOURCE(S): MARPAT 136:85627
GI



I

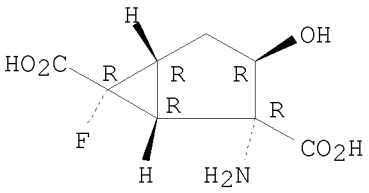
AB 2-Amino-6-fluorobicyclo[3.1.0]hexane-2,6-dicarboxylic acid derivs. represented by the general formula I [R1, R2 = H, alkyl, etc.; when R3 is OH, R4 is H; or R3R4 = bond] are prepared These compds. are useful as drugs, in particular, group 2 metabotropic glutamate receptor agonists having therapeutic and preventive effects on, for example, psychiatric diseases such as schizophrenia, anxiety, etc. (1R,2R,3R,5R,6R)-2-Amino-6-fluoro-3-hydroxybicyclo[3.1.0]hexane-2,6-dicarboxylic acid was prepared and its bioactivity was demonstrated.

IT 385372-18-9P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of bicyclo[3.1.0]dicarboxylic acid derivs. as group 2 metabotropic glutamate receptor agonists)

RN 385372-18-9 CAPLUS

CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-6-fluoro-3-hydroxy-, (1R,2R,3R,5R,6R)- (CA INDEX NAME)

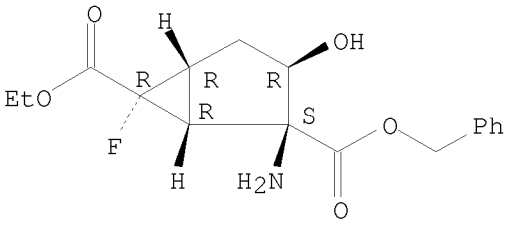
Absolute stereochemistry. Rotation (-).



IT 385372-31-6P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of bicyclo[3.1.0]dicarboxylic acid derivs. as group 2 metabotropic glutamate receptor agonists)

RN 385372-31-6 CAPLUS
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-6-fluoro-3-hydroxy-, 6-ethyl 2-(phenylmethyl) ester, (1R,2S,3R,5R,6R)- (CA INDEX NAME)

Absolute stereochemistry.



OS.CITING REF COUNT: 5 THERE ARE 5 CAPLUS RECORDS THAT CITE THIS RECORD (8 CITINGS)
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L17 ANSWER 3 OF 4 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2000:157966 CAPLUS
DOCUMENT NUMBER: 132:166520
TITLE: Stereospecific synthesis of 2-amino-bicyclo[3.1.0]hexan-2,6-dicarboxylic acid derivatives for use as metabotropic glutamate receptor ligands
INVENTOR(S): Adam, Geo; Huguenin-Virchaux, Philippe Nicolas; Mutel, Vincent; Stadler, Heinz; Woltering, Thomas Johannes
PATENT ASSIGNEE(S): F. Hoffmann-La Roche A.-G., Switz.
SOURCE: Ger. Offen., 22 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
DE 19941675	A1	20000309	DE 1999-19941675	19990901	<--
CH 694053	A5	20040630	CH 1999-1550	19990824	
US 6107342	A	20000822	US 1999-385935	19990830	<--
CA 2281272	A1	20000303	CA 1999-2281272	19990831	<--
GB 2341179	A	20000308	GB 1999-20579	19990831	<--
GB 2341179	B	20040218			
JP 2000086597	A	20000328	JP 1999-244167	19990831	<--
JP 3340409	B2	20021105			
SE 9903088	A	20000304	SE 1999-3088	19990901	<--
SE 520026	C2	20030513			
FR 2786768	A1	20000609	FR 1999-10971	19990901	<--
FR 2786768	B1	20041015			
IT 99MI1860	A1	20010301	IT 1999-MI1860	19990901	<--
IT 1313618	B1	20020909			
NL 1012963	A1	20000306	NL 1999-1012963	19990902	<--
NL 1012963	C2	20031023			

AU 9947327	A	20000316	AU 1999-47327	19990902 <--
AU 757939	B2	20030313		
AT 501853	A1	20061115	AT 1999-1514	19990902
BE 1014616	A3	20040203	BE 1999-595	19990903
PRIORITY APPLN. INFO.:			EP 1998-116670 A	19980903
OTHER SOURCE(S):	MARPAT 132:166520			

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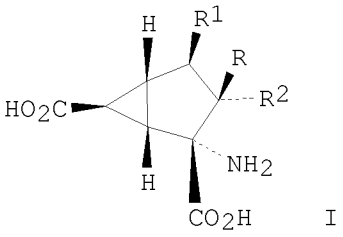


I

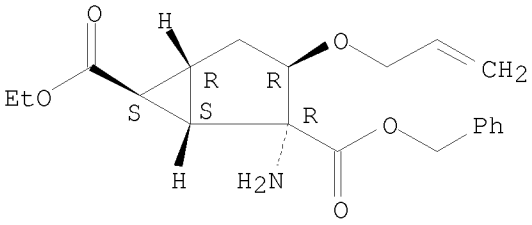
AB Title compds. [(I); R = OH, alkoxy, alkenyloxy, PhCH2O-, H, 2H, 3H; R1 = H, 3H; R,R1 = bond; R2 = H, 2H, 3H, OH, NH2] were stereospecifically prepared for use in treatment of neurol. conditions and psychiatric disturbances (no data). Thus, racemic Et (1α,5α,6α)-2-oxo-bicyclo[3.1.0]hexane-6-carboxylic acid was reacted with Ph bis((trifluoromethyl)sulfonyl)amine and the resulting triflate transformed into the racemic 2-ethyl-6-benzyl bicyclo[3.1.0]hex-2-ene-2,6-dicarboxylic acid, reaction of which with K2[OsO2(OH)4] gave stereospecifically the 1S,2S,3R,6S-diol, which could be isolated in 26% yield, at >99% enantiomeric excess. Preparation of the 2R-2-azido compound from the diol through a cyclic sulfate gave an intermediate which could then be alkylated, aminated, hydrogenated, de-esterified, or otherwise treated to give I, for use as ligands for metabotropic glutamate group II receptors.

IT 259134-78-6P 259134-79-7P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(stereospecific synthesis of 2-amino-bicyclo[3.1.0]hexan-2,6-dicarboxylic acid derivs. for use as metabotropic glutamate receptor ligands)

RN 259134-78-6 CAPLUS

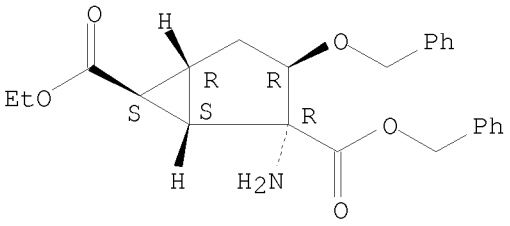
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-3-(2-propen-1-yloxy)-, 6-ethyl 2-(phenylmethyl) ester, (1S,2R,3R,5R,6S)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RN 259134-79-7 CAPLUS
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-3-(phenylmethoxy)-, 6-ethyl 2-(phenylmethyl) ester, (1S,2R,3R,5R,6S)- (CA INDEX NAME)

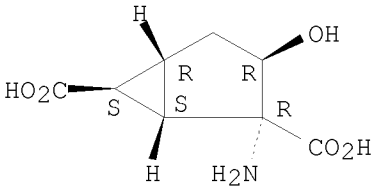
Absolute stereochemistry. Rotation (+).



IT 259134-85-5P 259134-86-6P 259134-87-7P
259134-88-8P 259134-89-9P 259134-94-6P
259134-95-7P 259134-96-8P 259134-97-9P
259134-98-0P 259135-00-7P
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(stereospecific synthesis of 2-amino-bicyclo[3.1.0]hexan-2,6-dicarboxylic acid derivs. for use as metabotropic glutamate receptor ligands)

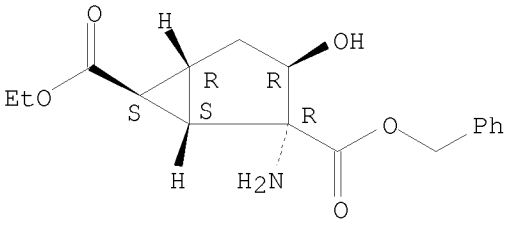
RN 259134-85-5 CAPLUS
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-3-hydroxy-, (1S,2R,3R,5R,6S)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



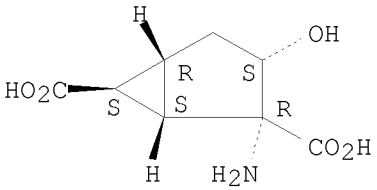
RN 259134-86-6 CAPLUS
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-3-hydroxy-, 6-ethyl 2-(phenylmethyl) ester, (1S,2R,3R,5R,6S)- (CA INDEX NAME)

Absolute stereochemistry.



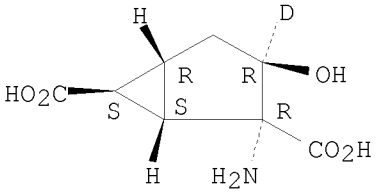
RN 259134-87-7 CAPLUS
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-3-hydroxy-, (1S,2R,3S,5R,6S)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



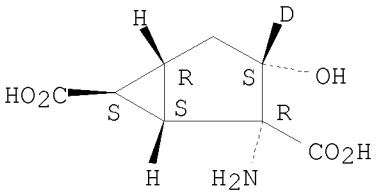
RN 259134-88-8 CAPLUS
CN Bicyclo[3.1.0]hexane-3-d-2,6-dicarboxylic acid, 2-amino-3-hydroxy-, (1S,2R,3R,5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



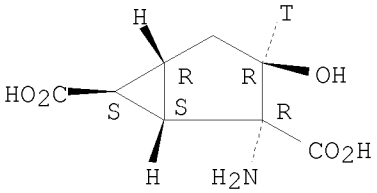
RN 259134-89-9 CAPLUS
CN Bicyclo[3.1.0]hexane-3-d-2,6-dicarboxylic acid, 2-amino-3-hydroxy-, (1S,2R,3S,5R,6S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



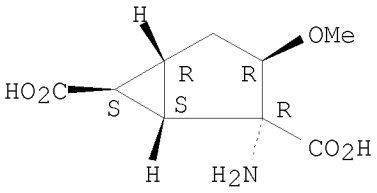
RN 259134-94-6 CAPLUS
CN Bicyclo[3.1.0]hexane-3-t-2,6-dicarboxylic acid, 2-amino-3-hydroxy-, (1S,2R,3R,5R,6S)- (CA INDEX NAME)

Absolute stereochemistry.



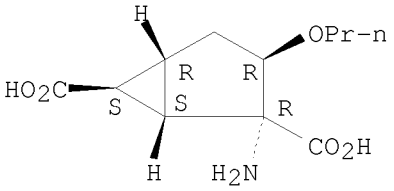
RN 259134-95-7 CAPLUS
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-3-methoxy-, (1S,2R,3R,5R,6S)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



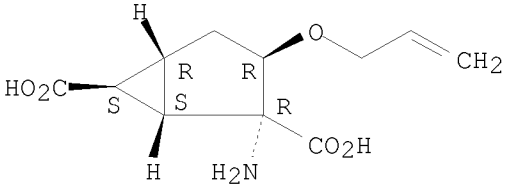
RN 259134-96-8 CAPLUS
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-3-propoxy-, (1S,2R,3R,5R,6S)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RN 259134-97-9 CAPLUS
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-3-(2-propen-1-yloxy)-, (1S,2R,3R,5R,6S)- (CA INDEX NAME)

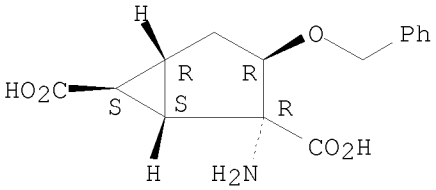
Absolute stereochemistry. Rotation (-).



RN 259134-98-0 CAPLUS
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-3-(phenylmethoxy)-,

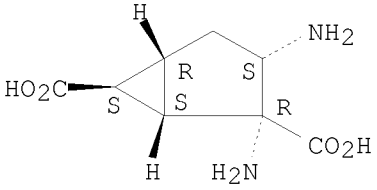
(1S,2R,3R,5R,6S)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (-).



RN 259135-00-7 CAPLUS
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2,3-diamino-, (1S,2R,3S,5R,6S)- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



OS.CITING REF COUNT: 10 THERE ARE 10 CAPLUS RECORDS THAT CITE THIS RECORD (27 CITINGS)

L17 ANSWER 4 OF 4 CAPLUS COPYRIGHT 2009 ACS on STN
ACCESSION NUMBER: 2000:68447 CAPLUS
DOCUMENT NUMBER: 132:93652
TITLE: Preparation of 2-aminobicyclo[3.1.0]hexane-2,6-dicarboxylates and related compounds as pharmaceutical intermediates and modulators of metabotropic glutamate receptor function.
INVENTOR(S): Baker, Stephen Richard; Monn, James Allen; Ezquerra Carrera, Jesus; Dominguez Fernandez, Carmen
PATENT ASSIGNEE(S): Eli Lilly and Company Limited, UK; Lilly, S.A.; Eli Lilly and Company
SOURCE: PCT Int. Appl., 48 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000004010	A1	20000127	WO 1999-GB2273	19990714 <--

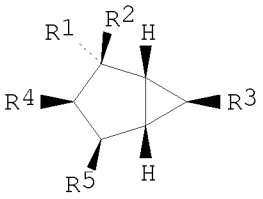
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN,

MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM,
TR, TT, UA, UG, US, UZ, VN, YU, ZW
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK,
ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG,
CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

CA 2338054	A1	20000127	CA 1999-2338054		19990714 <--
AU 9949223	A	20000207	AU 1999-49223		19990714 <--
EP 1097149	A1	20010509	EP 1999-933048		19990714 <--
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI					
JP 2002520406	T	20020709	JP 2000-560116		19990714 <--
PRIORITY APPLN. INFO.:			GB 1998-15542	A	19980717
			WO 1999-GB2273	W	19990714

OTHER SOURCE(S): MARPAT 132:93652

GI



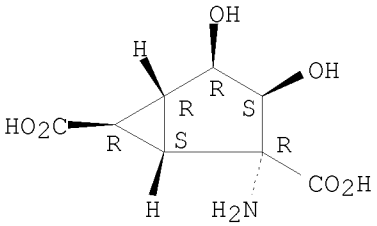
I

AB Title compds. [I; either R1 = N3, (protected) amino; R2 = (protected) carboxy; or R1 = trihalomethyl; R2 = OH; R3 = (protected) carboxy; either R4 = OR6 and R5 = OR7; or R4 and R5 = H or R4R5 = bond; ether R6 and R7 = H; or R6R7 = diol protecting group; provided that when R4 and R5 = H, R1 ≠ amino], were prepared s pharmaceutical intermediates and modulators of metabotropic glutamate receptor function (no data). Thus, ethoxycarbonylmethyldimethylsulfonium bromide in CHCl3 was treated with DBU and then with (-)-2,3-(cyclohexylidenedioxy)-4-cyclopentenone in CHCl3 followed by stirring overnight to give 96% Et (1S,3R,4R,5R,6S)-2-oxo-3,4-cyclohexylidenedioxybicyclo[3.1.0]hexane-6-carboxylate. This with CHCl3 in THF at -78° was treated with Li hexamethyldisilazide in THF followed by warming to room temperature to give 94% Et (1S,2S,3R,4R,5R,6S)-2-trichloromethyl-2-hydroxy-3,4-cyclohexylidenedioxybicyclo[3.1.0]hexane-6-carboxylate. Treatment of the latter with NaN3, 18-crown-6, and DBU in MeOH over 6 h gave 84% di-Me (1S,2R,3S,4R,5R,6S)-2-azido-3,4-cyclohexylidenedioxybicyclo[3.1.0]hexane-2,6-dicarboxylate. This was hydrogenated in EtOAc over Pd/C to give 71% of the corresponding amine, which was converted to (1S,2R,3S,4R,5R,6R)-2-amino-3,4-dihydroxybicyclo[3.1.0]hexane-2,6-dicarboxylic acid in several steps.

IT 254982-42-8P 254982-43-9P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation of 2-aminobicyclo[3.1.0]hexane-2,6-dicarboxylates and related compds. as pharmaceutical intermediates and modulators of metabotropic glutamate receptor function)

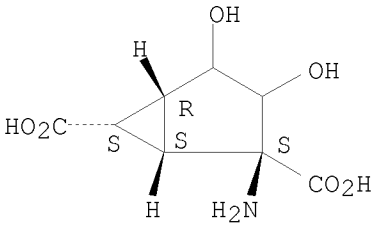
RN 254982-42-8 CAPLUS
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-3,4-dihydroxy-, (1S,2R,3S,4R,5R,6R)- (CA INDEX NAME)

Absolute stereochemistry.



RN 254982-43-9 CAPLUS
CN Bicyclo[3.1.0]hexane-2,6-dicarboxylic acid, 2-amino-3,4-dihydroxy-, (1S,2S,5R,6S)- (CA INDEX NAME)

Absolute stereochemistry.



OS.CITING REF COUNT:	3	THERE ARE 3 CAPLUS RECORDS THAT CITE THIS RECORD (3 CITINGS)
REFERENCE COUNT:	1	THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT